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Characterizing Patient Perceptions of Living with Geographic Atrophy: The Global Geographic Atrophy Insights Survey

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Background: Geographic atrophy (GA) is an advanced form of age-related macular degeneration leading to irreversible vision loss and negative impacts on quality of life.

Methods: To assess the experiences of living with GA, the Geographic Atrophy Insights Survey (GAINS) was conducted between October 12, 2021, and December 10, 2021, captured the responses of individuals ≥60 years with a self-reported GA diagnosis residing in the United States, Canada, Australia, and six European countries. Survey questions focused on the perceptions of individuals living with GA and covered six themes: speed of disease progression, effect on independence, impact on quality of life, emotional toll of GA, misconceptions and need for further education about GA, and clinician interactions. An exploratory comparison between participants with unilateral and bilateral GA was conducted.

Results: The survey included 203 individuals with a mean age of 70 years; 42% had bilateral GA. Most respondents (77%) agreed ("strongly" or "somewhat agreed") that GA impacted their vision faster than expected, and 68% agreed that it is hard to enjoy life fully the way they did before GA diagnosis. Regarding comparisons between individuals with bilateral and unilateral GA, both groups reported similar "major" or "moderate" negative impacts on their ability to drive (73% vs 75%, respectively), followed by the ability to read (66% vs 71%), and ability to travel as much as they would prefer (62% vs 62%). Among participants, 49% and 56% of respondents with bilateral and unilateral GA, respectively, reported major/moderate negative impacts on self-confidence and 40% of both cohorts reported major/moderate negative impacts on mental health.

Conclusion: Our survey provides further insight on the burden experienced by individuals living with GA. We find similar responses between unilateral and bilateral GA groups, highlighting the impact GA may have on an individual's quality of life even when only one eye is affected.

Keywords: geographic atrophy, age-related macular degeneration, atrophic AMD, burden of illness, quality of life, patient survey

Introduction

Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD) that results in progressive, irreversible vision loss.[1] It is estimated that over 5 million people worldwide were living with GA in 2021.[2] Advanced AMD presents as two distinct pathologies known as GA (or atrophic AMD) and neovascular AMD (nAMD, or "wet" AMD).[3] While individuals can develop GA or nAMD independently, these conditions can also occur simultaneously in the affected eye. Multiple treatment options exist for nAMD; however, GA has only recently received its first approved

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therapies (ie, pegcetacoplan and avacincaptad pegol) in the United States in 2023 which serve to slow the progression of GA.[4–7]

Individuals living with GA commonly develop scotomas in their visual field which may occur centrally, paracentrally, or both.[1,8,9] Visual impairment in GA occurs due to the loss of photoreceptors, retinal pigment epithelium (RPE), and underlying choriocapillaris in the retina.[10] This atrophy of retinal tissue (ie, atrophic lesion) results in progressive vision loss in those living with GA and manifests in symptoms such as decreased ability to determine contrast, detect color, and see at night.[1,11,12] Complicating matters further, individuals may be affected in a single eye (unilateral) or both eyes (bilateral).[13] Individuals diagnosed with unilateral GA can also develop bilateral GA; Kaplan-Meier estimates from 686 participants with unilateral GA in the Age-Related Eye Disease Study (AREDS) suggest that there is a 54% probability of developing bilateral GA eight years following a unilateral GA diagnosis.[14] Regarding the impacts of GA on visual decline, retrospective analysis of electronic medical records from over 1900 patients with GA by Chakravarthy et al indicated that 71% of individuals with bilateral GA had visual declines that would make them ineligible to drive with a median time to progression of 1.6 years and 16% became legally blind with a median time to progression of 6.2 years.[15] Indeed, GA is the fifth leading cause of blindness in the world and particularly affects elderly individuals.[16,17] A study by Patnaik et al revealed that composite scores for vision-related quality of life (QoL) showed similar negative impacts on general health between unilateral and bilaterally affected GA patients, while numerically worse scores were seen for bilateral patients for some subscale scores such as driving and role limitations.[18]

The visual decline that occurs due to GA can have dramatic impacts on the QoL for individuals living with this disease as well as loved ones that may be providing caregiver support, which may include negative impacts on one's ability to read, drive, and maintain a social life.[19,20] Few reports have documented the humanistic toll of GA on a person's QoL and well-being, and none have reported item-level comparisons between a robust sample size of unilateral and bilateral individuals with GA.[19] The aim of this survey was to capture and report on the prevalence of experiences among individuals living with GA related to their perceptions of GA, the effect that GA has on their lives, and their experiences with clinician interactions. To assess the burden of this disease when individuals are affected in one or both eyes, a post-hoc analysis was performed to compare responses between individuals with unilateral or bilateral GA.

Materials and Methods

Survey Overview

The Geographic Atrophy Insights Survey (GAINS) was conducted by the Harris Poll on behalf of Apellis Pharmaceuticals Inc. between October 12, 2021, and December 10, 2021. The survey was conducted among adults aged ≥60 years with a self-reported GA diagnosis. The survey was non-interventional in nature, was not used for treatment decisions, and was not conducted as a clinical trial for any endpoints. The responses from participants with GA were collected anonymously to ensure confidentiality.

Survey Design, Participants, and Recruitment Procedures

Survey data was collected by The Harris Poll online and via telephone in the United States, United Kingdom, France, Germany, Italy, Netherlands, Sweden, Canada, and Australia. Participants were recruited through recommendations by physicians or online panels and telephone databases of individuals who had agreed to participate in market research studies. The survey took approximately 30 minutes, on average, and online participants were compensated for their time according to local fair-market value guidelines. The survey broadly captured six themes of living with GA, including the speed of progression, emotional toll, effect on respondent's independence, impact on QoL, misconceptions and need for further education about GA, and clinician interactions (Supplemental File 1). Survey questions were reviewed by clinician researchers, relevant patient organizations, and expert pollsters local to the surveyed geographies to ensure that the questions were clinically relevant, patient-centered, appropriately balanced, and so that the meaning of each question was retained when translated between languages. Survey questions utilized responses that included numeric responses, single or multiple response picklist options, yes/no structure, unipolar scales, or a Likert-scale response

indicating their level of agreement with the question (eg, strongly agree, somewhat agree, etc.). Responses were reported on an item-level basis and a total item scoring system was not applied.

To be included in the survey, respondents were required to self-report a GA diagnosis with dry AMD in at least one eye, and to be experiencing at least three GA symptoms at the time of the survey (Supplementary Table S2). Respondents must have indicated that they had self-reported advanced atrophic AMD, advanced/late/late-stage dry AMD, or GA in one or both eyes. Respondents were required to currently, formerly, or have been suggested by an eye care professional (ECPs) to have done at least one of the following: take a high-dose formulation of antioxidant vitamins and minerals, stop smoking, maintain a healthy weight and exercise regularly, choose a healthy diet, manage other medical conditions, have check-ups of the retina regularly, or wear sunglasses with UV protection. These criteria were set to increase the generalizability of the findings by including participants that have been advised or are currently practicing healthy lifestyle habits that support their eyesight. Respondents were excluded if they had been diagnosed with glaucoma, Stargardt disease, or dementia. Patients were also excluded if they responded that they had ever (or were unsure if they had) received regular injections into the eye affected with GA every 4 to 6 weeks. Individuals with unilateral GA were excluded if they reported having nAMD in the same eye affected by GA.

Analysis of Survey Responses

The sampling precision of Harris online polls was measured by using a Bayesian credible interval, and the sample data is accurate to within ±7.8 percentage points using a 95% confidence level and ±6.5 percentage points using a 90% confidence level. To reflect the global perspective, findings were normalized with respect to a participant's country's total adult population (Supplementary Table S1); in other words, a proportionate post-weight was applied to adjust for the relative size of each country's adult population within the total adult population across all countries surveyed.[21] The adult population values for each country were obtained from the US Census Bureau's Current Population Survey and International Database.[22,23] Descriptive statistics were used to assess survey responses. A z-test with an alpha level of $p<0.05$ was used to detect statistically significant differences for survey responses between proportions of respondents reporting unilateral or bilateral GA. Statistical analysis was conducted using Quantum v5.8 software.

Results

The survey included 203 individuals (69% male, 31% female, Table 1) with GA with a mean age of 70 years (standard deviation [SD] of 6.3); the mean age (SD) for those with unilateral GA was 70.1 (5.82) and was 70.0 (6.96) for those with bilateral GA. The list of reported symptoms by participants and their relative prevalence is provided in Supplementary Table S2. Among all participants, the most commonly reported symptoms were needing a brighter light when reading (85%), an inability to drive at night (83%), and reduced central vision in one or both eyes (74%) (Supplementary Table S2). The mean time (SD) between the respondents' GA diagnosis and their participation in this survey was 4.5 (3.3) years; 24% of participants were diagnosed within the past 2 years, 39% diagnosed in previous 3–4 years, and 37% were diagnosed in the past 5 or more years. Importantly, 91% of respondents did not report a nAMD diagnosis, demonstrating that the responses overwhelmingly reflect the impact of living with GA and not other forms of AMD. Of respondents, 58% reported having unilateral GA (20% in left eye and 38% in right eye) and 42% responded having bilateral GA. Overall, respondents with bilateral GA were significantly more likely to report certain GA-related symptoms than individuals with unilateral GA ($p<0.05$, Supplementary Table S2).

Speed of GA Progression

The majority of respondents (77%) "strongly agree" or "somewhat agree" (23% and 54%, respectively) with the statement that GA impacted their vision faster than they expected (Figure 1). On average (SD), participants reported noticing their vision decline or worsen 2.4 (1.6) years following their GA diagnosis. Significantly more individuals with bilateral GA responded that their vision started to decline prior to their GA diagnosis than individuals with unilateral GA (40% vs 24%, $p=0.036$); the mean (SD) time that individuals noticed their vision decline following their GA diagnosis was 1.5 (1.3) years for bilaterally affected individuals and 2.7 (1.5) years for unilaterally affected individuals (Table 1).

Table 1 Characteristics of Survey Respondents

n (%)	Total N=203	Bilateral GA n=86	Unilateral GA n=117	P-value*
Sex				
Male	139 (69)	57 (67)	82 (70)	0.335
Female	64 (31)	28 (33)	35 (30)	0.335
Eyes affected by GA				
Left eye only	40 (20)	-	40 (34)	-
Right eye only	77 (38)	-	77 (66)	-
Both eyes	86 (42)	86 (100)	-	-
Wet AMD				-
Left eye only	-	-	-	-
Right eye only	3 (2)	2 (2)	1 (1)	-
Both eyes	9 (4)	9 (11)	-	-
Time between GA diagnosis and survey response				
Less than 1 year	3 (1)	2 (2)	1 (1)	0.422
1–2 years	46 (23)	22 (26)	24 (20)	0.232
3–4 years	79 (39)	37 (43)	42 (36)	0.080
5+ years	75 (37)	25 (29)	51 (44)	0.017
Time after diagnosis that respondents reported noticing their vision decline or worsen due to GA				
Has not started to decline/worsen	27 (13)	18 (21)	10 (8)	0.004
Prior to diagnosis	63 (31)	34 (40)	29 (24)	0.036
Less than 1 year	15 (7)	10 (12)	5 (4)	0.028
1–2 years	52 (26)	17 (20)	35 (30)	0.028
3–4 years	36 (18)	6 (7)	31 (26)	0.003
5+ years	11 (5)	1 (2)	9 (8)	0.023
Respondents reporting relying on a caregiver due to vision loss	109 (54)	38 (44)	72 (62)	0.022
Caregiver relationship[a,b]				
Spouse or Partner	87 (81)	25 (71)	62 (85)	0.012
Children	60 (55)	13 (37)	46 (64)	0.005
Sibling	19 (18)	2 (7)	17 (23)	0.062
Another relative	9 (9)	1 (3)	8 (12)	0.077
Close friend	7 (7)	3 (8)	4 (6)	0.340
Professional caregiver	6 (6)	4 (11)	2 (3)	0.051

Notes: The sample size (n) and percentages (%) for all rows are based on weighted data and therefore do not reflect the exact number of participant responses. *p-values are shown for comparisons between bilateral and unilateral GA cohorts. [a]Among respondents who reported relying on a caregiver. [b]Selected from all that apply.
Abbreviations: GA, geographic atrophy; AMD, age-related macular degeneration.

Impact of GA on Independence and Quality of Life

When asked about the impact of GA-related visual impairment, 68% of all participants agreed (16% "strongly" and 52% "somewhat" agreed) with the statement that their visual decline impacted their QoL and independence worse than they expected (Figure 1). Respondents that reported relying on a caregiver after diagnosis (46% of all respondents) started receiving caregiver support 2.6 years on average (SD of 1.6) after their GA diagnosis. Of all participants, 72% reported falling or injuring themselves; 92% of all participants that fell believed that at least some proportion of these falls occurred due to their vision loss related to GA (Supplementary Table S1). In general, participants with GA in one or both eyes reported similar responses for how GA had negatively impacted specific aspects of their lives (Figure 2), as well as similar responses on the activities they had given up entirely or reduced time doing (Table 2). Of these responses, the only statistically significant differences that were detected between individuals with unilateral and bilateral GA were responses related to their personal relationships.

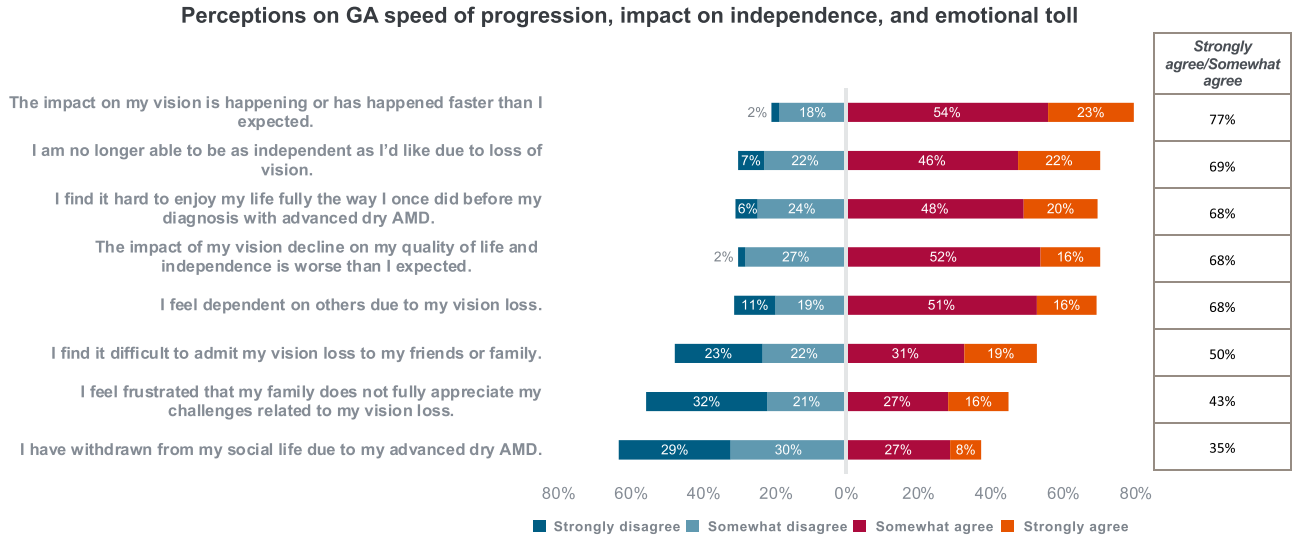

Figure 1 Participant responses to questions related to the themes of speed of GA progression, impact on independence, and emotional toll. Participants that responded "Not applicable" or "Unsure/Refused" comprise the difference between the sum of agree/disagree responses and 100%; these cases represent less than 5% of responses. Total values for strongly agree/somewhat agree reflect rounded totals.

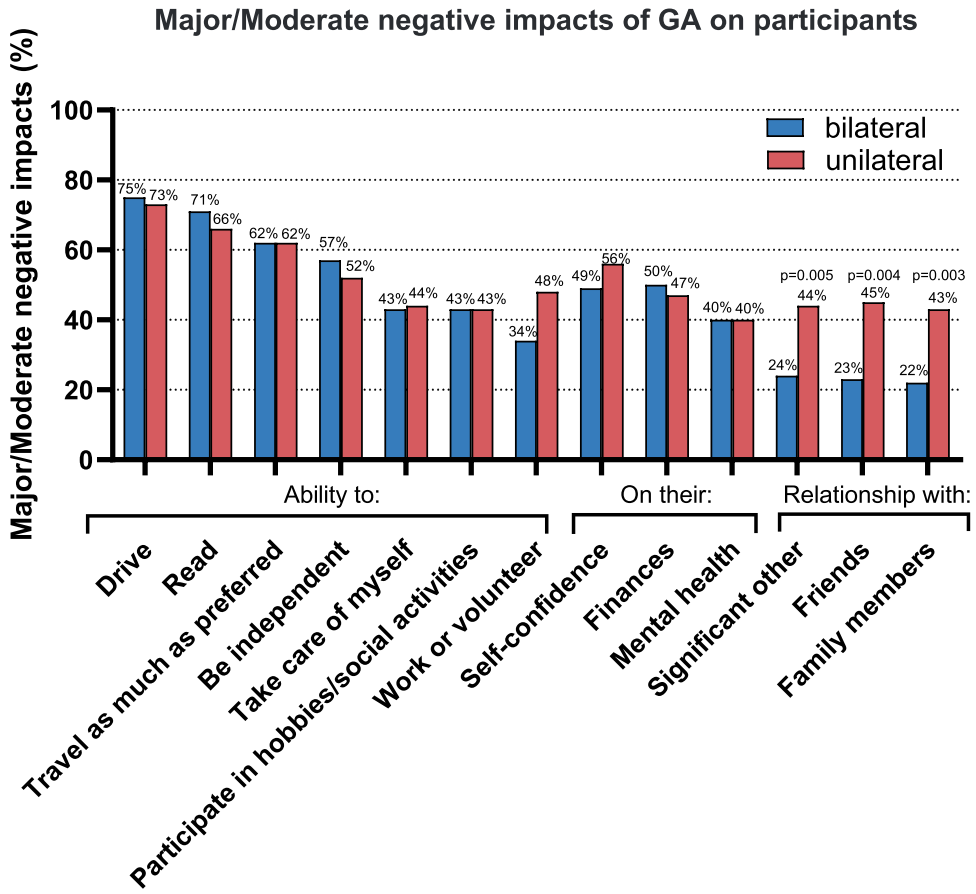

Figure 2 Percentage of participants with unilateral and bilateral GA that reported major or moderate negative impacts when asked about how GA has impacted certain aspects on their ability to perform tasks of daily living, emotional well-being, or effects on their relationships.

Table 2 Participants That Responded They Had Given Up Entirely/Reduced Time Spent Doing Certain Activities Due to Their Vision Loss as a Result of GA

Activities, n (%)	Total N = 203	Bilateral GA n = 86	Unilateral GA n = 117	P-value*
Driving at night (in the dark)	141 (70)	66 (77)	76 (64)	0.043
Driving at any time of day	121 (60)	56 (66)	65 (55)	0.107
Traveling	113 (56)	47 (55)	66 (56)	0.305
Working or volunteering	92 (45)	39 (46)	53 (45)	0.436
Exercising	87 (43)	38 (44)	49 (42)	0.447
Pursuing hobbies	75 (37)	34 (40)	41 (35)	0.228
Completing household chores[a]	73 (36)	29 (34)	43 (37)	0.328
Shopping[b]	71 (35)	34 (40)	37 (31)	0.101
Reading text in printed materials[c]	69 (34)	26 (30)	43 (36)	0.156
Reading text on a screen[d]	67 (33)	27 (32)	40 (34)	0.375
Maintaining personal grooming[e]	53 (26)	22 (25)	32 (27)	0.355
Watching TV or movies	53 (26)	23 (27)	30 (26)	0.483
Socializing with friends or family	43 (21)	11 (13)	31 (27)	0.011

Notes: The sample size (n) and percentages (%) for all rows are based on weighted data and therefore do not reflect the exact number of participant responses. *p-values are shown for comparisons between bilateral and unilateral GA cohorts. [a]For example, cleaning, cooking or yard work. [b] For example, for clothes or groceries. [c]For example, books, newspapers or bank account statements. [d]For example, computers, phones, tablets or social media. [e]For example, shaving, brushing hair or clipping nails.
Abbreviation: GA, geographic atrophy.

Emotional Toll of GA

Of all participants, 68% (20% "strongly" and 48% "somewhat") agreed with the statement that they find it hard to enjoy their life fully the way they did before their GA diagnosis (Figure 1). When asked to select adjectives from a pre-specified list to describe how individuals feel due to their GA-related vision loss, participants reported feeling anxious (46%) and powerless (39%); only 19% of respondents selected hopeful (Supplementary Table S3). When asked about the negative impact of GA on certain aspects of their life, 49% of bilaterally- and 56% of unilaterally affected individuals reported major/moderate negative impacts on their self-confidence (20% "major" and 29% "moderate" for bilateral; 15% "major" and 41% "moderate" for unilateral). When asked about the impact of GA on mental health, 40% of bilateral and unilateral affected individuals reported major/moderate negative impacts on their mental health (11% "major" and 28% "moderate" for bilateral; 13% "major" and 27% "moderate" for unilateral) (Figure 2). Compared to individuals with bilateral GA, significantly more participants with unilateral GA reported major/moderate negative impact on relationships with spouses or significant others (44% vs 24%, p=0.005; 16% "major and 28% "moderate" for unilateral; 5% "major" and 19% "moderate" for unilateral) and family members (43% vs 22%, p=0.003; 8% "major" and 35% "moderate" for unilateral; 7% "major" and 15% "moderate" for unilateral).

Misconceptions and Need for Further Education

When asked about the need for GA-related education, 86% of respondents (30% "strongly" and 55% "somewhat) agreed with the statement that they wished there were more educational materials available for patients and caregivers (Figure 3). Of all participants, 83% (36% 'strongly' and 47% 'somewhat') agreed with the statement that they wished they had more information about their condition at the time of their diagnosis to prepare them for the impact of disease progression. Regarding GA-related misconceptions, 76% of respondents (20% 'strongly' and 55% somewhat)" attributed their vision loss to a natural part of aging. When asked about the understanding of GA-related information, 32% of all respondents also incorrectly responded "true" that the rate of disease progression is the same for most patients, with 22% responding with "not sure" (Supplementary Table S1).[12]

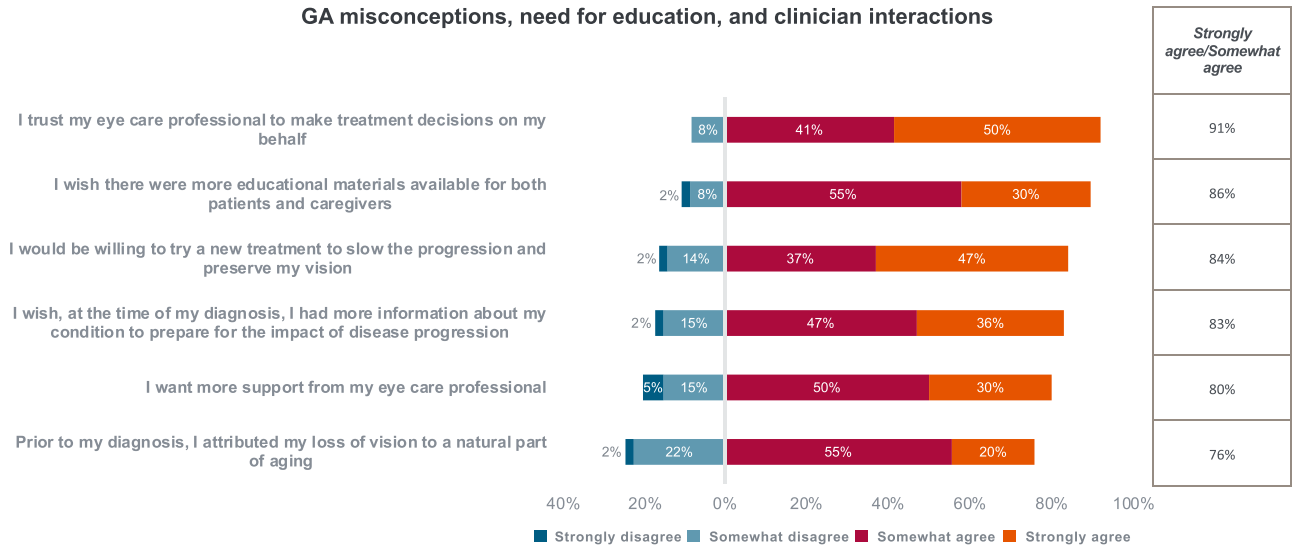

Figure 3 Perceptions of individuals with GA regarding the need for further GA-related education and interactions with eye care professionals. Participants that responded "Not applicable" or "Unsure/Refused" comprise the difference between the sum of responses and 100%; these cases represent less than 5% of responses. Total values for strongly agree/somewhat agree reflect rounded totals.

Interfacing with Clinicians

When asked to select all that apply for recalling what prompted their GA diagnosis, 67% of participants indicated that they were diagnosed due to a routine eye exam and 51% reported seeking an appointment with an ECP due to changes in their vision (Supplementary Table S1). When asked about the types of ECPs seen by participants, individuals most frequently visited a general ophthalmologist for GA-related care (53%), followed by retina specialists (47%), low vision specialists (40%), and optometrists (37%). Notably, 84% of participants (47% "strongly" and 37% "somewhat") agreed with the statement that they would be willing to try new treatments to slow the progression and preserve their vision loss.

Discussion

Individuals diagnosed with GA must live with progressive atrophy of retinal tissue. This global survey is the largest comprehensive survey to date that explores and reports the prevalence of GA-related experiences and perceptions of those living with GA. Notably, this survey was conducted prior to the regulatory approval of any GA-related treatments and our findings reflect the responses of those living with GA when treatment is not available. The findings from this survey exemplify the many impacts that GA-related visual decline has on the lives of individuals, the need for improved educational materials related to GA, and the experiences of interacting with clinicians. Importantly, our results demonstrate many similarities exist in the responses of individuals with unilateral and bilateral GA, indicating that the impact of GA on a person's life is similar, in some aspects, regardless of whether only one eye is affected from this disease.

Previous studies have provided insight on the impact that GA has on the lives of people with this disease and have laid the groundwork for the current survey. Importantly, the majority of prior work focused on individuals with any form of AMD and did not distinguish between individuals diagnosed with sub-types of late-stage AMD (ie, GA and nAMD).[24,25] The importance for distinguishing individuals diagnosed with nAMD and GA was recently demonstrated in a study by Ahluwalia et al, which revealed significant differences in disease progression between patients with GA and nAMD.[26] As mentioned previously, nAMD and GA represent distinct pathologies that are further demonstrated by the use of separate therapeutic strategies targeting the varying mechanisms for nAMD and GA.[4,27] The need to distinguish individuals with GA from those with other AMD sub-types has also been recognized by recent studies that investigated the effect on QoL; however, these studies have been limited by small sample sizes or composite scoring that poorly represents the humanistic toll of GA. Caswell et al provided a thorough qualitative examination of a single patient with GA and their caregiver providing new perspectives on the impact of GA on an individual and their family.[20]

Madheswaran et al performed a qualitative study on 10 participants with bilateral central vision loss due to GA and identified themes that negatively impacted GA patients' daily activities of living, socialization, and psychological well-being.[28] Sivaprasad et al identified several factors that were negatively impacted by GA, such as driving; however, this study included only 16 participants which limited its ability to depict the relative experiences that can occur across the spectrum of patients with GA.[19] Patel et al showed that patients with GA exemplified worse composite scores in QoL compared to individuals without GA in sub-scales such as near and distance activities.[29] Further, findings from Patnaik et al indicated that composite subscale scoring for certain QoL related measures, such as role limitations, dependency, and driving, were numerically worse in bilateral patients with GA than those with unilateral GA.[18] While composite sub-scale scoring in Patel et al and Patnaik et al provide a quantitative impact assessment, this approach lacks the utility of depicting the humanistic toll that GA has on the lives of these patients. Collectively, our findings agree with previous studies that GA has significant deleterious effects on the lives of those living with GA. Our findings provide new insights on the experiences of individuals with GA and is the first study to indicate that these experiences may not largely differ between individuals with unilateral and bilateral GA.

Importantly, our findings reveal that respondents largely reported similar experiences between those with unilateral and bilateral GA and provides new insights on this disease. While respondents with bilateral GA were significantly more likely to experience certain GA-related symptoms than those with unilateral GA, our survey reveals that individuals with unilateral and bilateral GA had similar negative impacts on their independence, emotional well-being, and mental health. This is further reflected by similar responses between individuals with bilateral and unilateral GA on the amount of time they had decreased spending on certain activities such as driving, traveling, working, or exercising. Given that significantly more bilateral GA respondents reported noticing their vision decline prior to their diagnosis, it is plausible that the negative effects of GA-related vision loss may impact individuals with bilateral GA sooner than those affected in only one eye. However, our survey did not collect responses on which eye was a participant's better seeing eye, and it is possible that responses may have varied between respondents (particularly with unilateral GA) depending on the quality of vision in their better seeing eye and the eye affected by GA. In addition, our findings revealed that significantly more respondents with unilateral GA reported major/moderate negative impacts on their relationships with their significant others, friends, and family members. It is unclear what may drive these differences, and future research is needed to further elucidate these findings. Nonetheless, our findings indicate that the majority of responses were similar between individuals with unilateral and bilateral GA and suggests that GA-related vision loss may impart similar detrimental effects on an individual's QoL regardless of being bilaterally or unilaterally affected.

There are several important considerations that may have played a role in the findings of similar responses between those with unilateral and bilateral GA. First, the inclusion criteria of requiring all participants to be experiencing 3 or more GA-associated symptoms may have limited the ability to capture patients with mild symptoms across both cohorts. Prior evidence from Varma et al has indicated that moderate/severe unilateral visual impairment (as determined by best-corrected visual acuity [BCVA]) has comparable effects on QoL to mild bilateral visual impairment.[30] However, prior evidence has demonstrated that measurements of visual acuity underestimate the visual dysfunction that occurs with GA.[12,31,32] Contrast sensitivity is a common symptom of GA, and contrast sensitivity has been shown to correlate better with subjective visual impairment and vision-related QoL than measures of visual acuity.[33] In support of the potential impact on QoL when considering visual acuity or alternative GA-related symptoms, Sivaprasad et al found similar functional impacts on QoL in bilaterally affected GA patients when sub-groups were partitioned into those with better or worse than 20/100 BCVA.[19] Hence, it is plausible that GA-associated symptoms outside of decrements in visual acuity may have impacted the perceptions of the included participants, especially given that these individuals had experienced an extensive time of living with GA (mean time since diagnosis of 4.5 years). Additionally, our current approach utilized item-level reporting in order to convey a humanistic perspective of the impacts of GA. This approach may lack granularity capable of discerning numerical differences between unilateral and bilateral GA cohorts. For instance, our findings show that 75% of bilateral and 73% of unilateral participants reported major or moderate negative impacts on their ability to drive; however, 77% of bilateral and 64% of unilateral participants responded that they had given up entirely or reduced time spent driving at night (in the dark). While it is possible that composite scoring could reveal differences between the two cohorts, it is important to recognize that this approach lacks the empathetic perspective of

how patients with GA perceive the impact of this disease. In this regard, revealing numerical differences between cohorts via composite scoring across multiple questions would not negate the findings of the current survey: that underlying negative impacts are persistent across symptomatic participants with GA regardless of being unilaterally or bilaterally affected.

Our findings add to the existing literature on the effects of GA on QoL by reporting on the prevalence of GA-related experiences in those living with GA. GA has a profound impact on an individual's independence with 70% of individuals having given up entirely or reduced time driving at night. In addition, 43% of participants report major/moderate negative impacts on their ability to participate in hobbies with 37% of respondents having given up entirely or reduced time pursuing their hobbies. Notably, a prior study on 819 patients treated for any form of low-vision (eg, glaucoma, diabetic retinopathy, etc.) in the United States has shown that less than 10% report difficulties with performing hobbies compared to 43% who report major/moderate negative impacts in the current study.[34] This comparison to the broader spectrum of vision loss disorders highlights the extent that GA negatively impacts individuals and the unique impact of GA-related vision loss. Declining independence can also result in many GA patients relying on assistance from caregivers. Our findings for caregiver support in individuals living with GA is higher than previously reported for all AMD patients, ie, not stratified by subtype; Schmier et al reported that ~36% of individuals with AMD relied on support from caregivers, of which 87% was from informal support (ie, family or friends).[35] Our survey indicated that 54% of respondents relied on caregiver support with 94% of these respondents relying on informal support.[35] This is an important consideration, because relying on informal care may also negatively impact those responsible for caregiving.[20]

Our findings indicate that individuals living with GA overwhelmingly agree that there is a need for further GA-related education, as well as more support from their ECP. Prior reports have indicated that the general population, clinicians, and ophthalmologists may commonly underestimate the impact of AMD on QoL.[36] Hence, further education on the impact of GA on patient QoL may be beneficial for both individuals living with GA and clinicians. Prior studies comparing the effect of AMD with poor vision to other diseases suggest that reductions in QoL are comparable to catastrophic health conditions such as prostate cancer or ischemic cerebrovascular accidents.[36,37] GA patients have reported receiving little information following their diagnosis and have had to rely on information from friends and family.[38] These prior studies in conjunction with our findings of the multi-faceted impacts that GA has on individuals highlight a significant unmet need for supporting patients affected by GA.

Misunderstandings about GA and its impact on QoL may arise due to the spectrum of symptoms that occur amongst individuals. GA-related vision loss varies between individuals and can initially occur in their central or paracentral field of vision and progress to affect both fields.[8,9] Complicating matters further, scotomas present differently amongst GA patients;[39] some individuals may have scotomas that allow central acuity but provide poor paracentral acuity which may prevent reading fluently if they are too large to be focused on. A classic example of this is that magnification of letters or words can exacerbate the inability to read, whereas some individuals may be able to read small print with better ease. In addition, individuals living with GA can face challenges in detecting color, determining contrast, adjusting to changes in light, recognizing faces, as well as experiencing visual hallucinations known as Charles Bonnet Syndrome.[40,41] In reference to our findings, 85% of participants reported a need for brighter light when reading, with 60% reporting decreased intensity of colors and 43% reporting distortion (eg, straight lines appearing to be bent). Hence, the range and broad variance of GA symptoms presented by patients makes it difficult to pinpoint the nature of their vision loss. Our survey did not collect information related to the lens status of the eye affected by GA (ie, pseudophakia or phakic), which may have also affected the symptoms experienced by individuals captured in our survey. Nonetheless, this difficulty in fully characterizing vision loss also applies to traditional measurements used to assess eye function; Schmitz-Valckenberg et al demonstrated that best corrected visual acuity (BCVA) measurements do not correlate well with GA disease progression.[12] Collectively, GA presents a difficult challenge for clinicians and patients to describe the range of symptoms that may occur in those diagnosed with GA.

Notably, our findings revealed a trend for several misconceptions in those living with GA that may arise due to a lack of information regarding GA. In particular, GA is often described to progress slowly by the medical community and scientific literature.[1,3,8,42,43] However, our findings reveal that individuals living with GA believe that GA-related visual decline occurs faster than they anticipated. While GA progression may not occur as quickly as some chronic diseases, it

is challenging to quantify the time that remains for each affected person's central vision. The current survey also shows that individuals living with GA may have misunderstandings of their diagnosis such as attributing their vision loss to a natural part of aging. These findings indicate that careful consideration should be taken by ECPs when estimating a timeframe for GA progression and for describing the cause of GA-related visual declines.

Survey Limitations

There are several limitations for the current survey that warrant consideration. First, a global survey was utilized to capture responses from a large cohort of affected patients and our findings were subject to limitations of survey data such as selection bias and recall bias. Our approach did not utilize a previously validated visual functioning and QoL survey, and instead relied upon a targeted survey tailored for GA in order to collect valuable information not captured by existing tools (eg, perception of speed of GA progression). Although not previously validated, this survey was developed through collaboration with leading ophthalmologic clinicians, patient organizations, and expert pollsters across the varying surveyed geographies to ensure that questions were clinically relevant, patient-centered, appropriately balanced, used plain language, and so that the meaning of each question was retained when translated between languages. The findings from our survey also reflected experiences of living with GA without available treatment; the recent Food and Drug Administration (FDA) approval of GA therapeutics may affect future outcomes and experiences of individuals living with GA.[4]

The survey also lacked validation against medical records or physician perspectives and relied on self-reported diagnoses. However, several measures were taken to increase the specificity of GA among survey responders, including providing clarifying statements for correctly identifying GA, multiple phrases that could be perceived by participants as interchangeable to GA, and requiring participants to be experiencing 3 or more symptoms associated with GA. Notably, the requirement to report 3 or more GA-related symptoms may have limited inclusion of participants with mild cases of GA, and the survey may represent populations with more severe GA that exhibit a higher symptomatic burden. In addition, an exhaustive list of alternative ocular disorders were not included as exclusion criteria in order to avoid any confusion that could occur among participants and to allow for increased survey focus on correctly identifying patients with GA. As there were no treatments available for GA at the time of the survey, the exclusion criteria for those that "had ever received regular injections into the affected eye" was used as a proxy for alternative ocular diseases that may have caused visual impairments to the extent that treatment was warranted. A small portion of bilateral participants with nAMD (12.8% among all bilateral participants) was included in the survey results, and the survey did not collect information regarding participants better seeing eye or lens status (eg, pseudophakia); these variables may have impacted participant responses. Future studies should consider including these considerations, as these points may result in differences among individual's response. However, our approach provided a robust sample size that captured participant responses across a global perspective. Our findings were consistent across geographies highlighting the persistent impacts of GA. In light of the recent approval of GA therapies in the United States, future studies assessing differences that may occur across geographies with varying healthcare access may be an important consideration for future studies.

The mean age of respondents for our survey was 70 years; however, prevalence data indicates that individuals aged 85–89 are most affected by GA which is older than the cohort captured in our survey.[17] Because this is a progressive disease, it is plausible that older participants may report more negative effects of GA and this consideration warrants further investigation. The survey was also designed for most respondents to take approximately 18–23 minutes which restricted the number of questions and follow-up questions. However, the question topics were selected based on themes identified by previously published work utilizing in-depth interviews as well as from clinician insight.[19] Our findings could have been affected by underlying respondent characteristics such as educational status, social status/network, and familial background; these points were not assessed by our survey and are a limitation. Lastly, the statistical approach (ie, z-test) was utilized to provide insights into potential differences between groups. As the goal was to provide clear and interpretable interpretations of the patient experience, advanced statistical modeling was not applied. The study findings had an 85% power and 95% confidence to detect a difference of 11% between groups. Potential differences less than 11% between individuals with unilateral and bilateral GA would not have been statistically detected with the current approach.

Conclusion

This global survey from over 200 individuals with GA provided a robust quantitative description of the impact of GA to date. Our findings demonstrate that GA has broad negative impacts on individual's QoL by decreasing their independence and diminishing their emotional well-being. In addition, our results also highlight that GA-related visual decline affects those living with GA earlier than they often expect. The findings from this survey indicate the need for further GA-related educational resources for individuals living with GA and continued support from ECPs, which represents an interesting area for future research to identify optimal approaches for supporting these patients. Importantly, our findings revealed many similarities between individuals with symptomatic unilateral and bilateral GA; this lack of difference in respondent perceptions suggests that the negative impacts of GA may occur even if only one eye is affected. Notably, respondents overwhelmingly agreed with the statement that they would be willing to try new treatments to slow the progression and preserve their vision loss. While grouping Likert responses (eg, strongly and somewhat agree) exemplify the general trend in patient experiences, it is also important to consider the relative impact that GA may have on individual patients. Future research exploring factors associated with the varying perceived degrees of impact of GA may be a useful area of future research to better understand patient needs. Overall, our findings provide greater insight into the burden of this disease so that clinicians and patients can better navigate and manage GA.

Data Sharing Statement

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

The survey was non-interventional in nature, was not used for treatment decisions, and was not conducted as a clinical trial for any endpoints. All respondents provided informed consent, and the survey was conducted in accordance with the relevant guidelines and regulations. The study complies with the Declaration of Helsinki. The survey did not require ethics approval as the project falls under Office for Human Research Protections (OHRP) Exempt Categories 45 CFR 46.101(B). Participant responses were collected anonymously to ensure confidentiality.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Sophie Bakri is an employee of the Mayo Clinic and reports consulting for AbbVie, Adverum, Allergan, Amgen, Annexon, Apellis, Aviceda, Eyepoint, Ilumen, Iveric bio, Kala, Genentech, Neurotech, Novartis, Outlook, Pixium, Regenxbio, Regeneron, Rejuvitas, Revana, Roche, Therapeutix, VoxelCloud, and Zeiss. Christian Brinkmann reports consulting for AbbVie, Afidera, Alimera, Apellis, Bayer, Novartis, SandozHexal, Santhera, Teleon. Amy Mulvey and Kathy Steinberg are employees of The Harris Poll, which was a paid contractor to Apellis Pharmaceuticals. Roz Katz and

Sujata Sarda are employees of Apellis Pharmaceuticals, Inc and current equity holders in the publicly traded Apellis Pharmacueticals, Inc company. At the time of the study, Pooja Vatsyayan was an employee of Apellis Pharmaceuticals, Inc and equity holder in the publicly traded Apellis Pharmaceuticals, Inc company. Nancy Holekamp is currently employed by Roche Pharmaceuticals, consults with Apellis Pharmaceuticals, Inc. 4DMT. AGTC, AbbVie/Allergan, Annexon, Bausch and Lomb, Bayer, Biogen, Boehringer, Cardinal, Clearside Biosciences, EyePoint Pharmaceuticals, Genentech, Gyroscope, Medpace, Medscape, Nacuity, NGM, Notal Vision, Novartis, Ocuphire, Outlook Therapeutics, Regeneron, Roche, Thea Laboratoires, Stealth Biosciences, and Vial and grants from Roche, Genentech, and Notal Vision.

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