Acta Ophthalmologica



# Visual complaints of patients with glaucoma and controls under optimal and extreme luminance conditions

Ronald A. J. M. Bierings,[1] Frideric L. P. van Sonderen[2] and Nomdo M. Jansonius[1]

[1]Department of Ophthalmology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
[2]Department of Health Sciences, Health Psychology Section, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

**ABSTRACT.**

***Purpose:*** **To determine (i) whether, compared to controls, visual complaints of glaucoma patients are more pronounced under extreme luminance conditions than in the optimal luminance condition and (ii) whether complaints belonging to different extreme luminance conditions are associated.**

***Methods:*** **We developed a luminance-specific questionnaire and sent it to 221 glaucoma patients (response rate 81%); controls (182) were primarily their spouses. Median (interquartile range) mean deviation of the visual field of the patients' better eye was −4.5 (−10.7 to −1.9) dB. Questions were addressing visual performance under five luminance conditions: presumed optimal (outdoor on a cloudy day), low, high, sudden decrease and sudden increase. We compared percentages of patients and controls who reported visual complaints while performing activities under different luminance conditions.**

***Results:*** **Percentages of patients and controls with visual complaints were 4 versus 0% ($p = 0.02$) for optimal luminance and 48 versus 6% ($p < 0.001$), 22 versus 1% ($p < 0.001$), 32 versus 1% ($p < 0.001$) and 25 versus 3% ($p < 0.001$) for low, high, sudden decrease and sudden increase in luminance. Within the group of glaucoma patients, the frequency of complaints increased significantly with increasing disease severity at a Bonferroni-corrected p value of 0.003 for all but one ($p = 0.005$) luminance-specific questions that addressed extreme luminance conditions.**

***Conclusion:*** **The concept of (early stage) glaucoma as an asymptomatic disease is only valid with optimal luminance. Differences in visual complaints between glaucoma patients and controls are greater under extreme luminance conditions, especially in the dark. The fact that the cases were aware of their diagnosis could have induced bias.**

**Key words:** adaptation – dark adaptation – glaucoma – luminance – quality of life – screening

Acta Ophthalmol.



doi: 10.1111/aos.13695

## Introduction

Glaucoma is a chronic and progressive eye disease characterized by loss of retinal ganglion cells (RGCs) and subsequent visual field loss. Visual field loss in glaucoma has traditionally been described as asymptomatic, peripheral visual field loss (Duke-Elder 1969). Although glaucoma indeed seems to be an asymptomatic disease in an early stage, glaucoma patients do report complaints; not related to peripheral visual field loss but to visual performance under extreme (low, high or changing) luminance conditions (Lee et al. 1998; Nelson et al. 1999; Janz et al. 2001a,b; Tatemichi et al. 2012; Hu et al. 2014). Complaints under extreme luminance conditions suggest impaired dark and light adaptation in glaucoma, which is an intriguing finding, because the rods and cones rather than the RGCs are the primary site of adaptation. A thorough understanding of the complaints could thus be important for a better understanding of the patient, the physiology of the retina, the pathophysiology of glaucoma and for improving diagnostic tests.

An increase in complaints under extreme luminance conditions is, in itself, not a surprise – this may also occur in healthy subjects; the question is whether the difference in visual complaints between glaucoma patients and healthy subjects is more pronounced under extreme luminance conditions compared to the optimal luminance condition. To address this question, it is necessary to have both an appropriate control group and a questionnaire with an extensive set of luminance-specific questions. None but two (Lee et al. 1998; Tatemichi et al. 2012) of the earlier studies did include a control group; without exception, earlier studies only included a subset of luminance conditions and questions regarding the optimal luminance

condition were always omitted. Another important question is whether complaints under low, high and changing luminance conditions go together (and may be thus related to a single underlying defect) or may appear in different proportions in different patients. Finally, if indeed the difference in visual performance between glaucoma patients and controls is more pronounced under extreme luminance conditions than under the optimal luminance condition, it might be better to perform diagnostic tests under extreme luminance conditions.

The aim of this study was to determine (i) whether, compared to controls, visual complaints of glaucoma patients are more pronounced under extreme luminance conditions than in the optimal luminance condition and (ii) whether complaints belonging to different extreme luminance conditions are associated. For this purpose, we performed a questionnaire study with an extensive set of luminance-specific questions amongst a large group of glaucoma patients and controls.

# Materials and Methods

### Study population and data acquisition

We sent a questionnaire by mail to 221 glaucoma patients with primary open-angle glaucoma, pseudoexfoliation glaucoma or pigment dispersion glaucoma. Patients were selected from the database of the Groningen Longitudinal Glaucoma Study, an observational cohort study conducted in our department (Heeg et al. 2005). We approached those participants who still were regular visitors of the outpatient clinic, were followed with standard automated perimetry [SAP; Humphrey field analyzer (HFA) 30-2 SITA; Carl Zeiss Meditec AG, Jena, Germany] and had a reproducible visual field defect on SAP in at least one eye, defined as a scotoma according to the LTG-P criterion (Katz et al. 1991) or a glaucoma hemifield test 'outside normal limits'. For descriptive statistics, the patients were stratified into early, moderate or severe glaucoma, using the mean deviation (MD) value of the better eye (eye with the higher MD value; Freeman et al. 2008; Gutierrez et al. 1997; Kulkarni et al. 2012; Mills et al. 2001; Peters et al. 2015; van Gestel et al. 2010). As cut-off points between the strata we employed -6 and -12 dB. For the classification, we used the most recent visual field test result. The median [interquartile range (IQR)] time window between this visual field and the questionnaire completion was 6 (2–14) months. We did not exclude visual fields based on reliability (to keep the time window as short as possible). The percentage of false-positive responses, the only reliability index that is significantly associated with the MD (Bengtsson & Heijl 2000; Junoy Montolio et al. 2012), was ≤10% in 165 of 178 glaucoma patients who returned the questionnaire. The median (IQR) percentage of false-positive responses was 13 (12–17) % in the remaining 13 patients. Patients were not selected with regard to their glaucoma stage.

Two questionnaires were sent to each patient; they were asked to complete one questionnaire and to give the other to their spouse, neighbour, friend, etc. (no consanguinity), who served as control. Patients and controls were explicitly asked to fill in the questionnaire independently. As the number of returned patient questionnaires exceeded the number of control questionnaires, additional controls were recruited from a recent case–control studies conducted in our department (Junoy Montolio et al. 2016). Controls were asked to confirm that they (i) did not have relatives with high eye pressure or glaucoma and (ii) did not receive regular checkups by an ophthalmologist for high eye pressure or glaucoma. In this way, we assured a glaucoma prevalence of <1% amongst the controls (Wolfs et al. 2000).

The ethics board of the University Medical Center Groningen (UMCG) approved the study protocol. All participants provided written informed consent. The study followed the tenets of the Declaration of Helsinki.

### Questionnaire

The questionnaire was developed to explore visual complaints during activities of various difficulty, under optimal and extreme luminance conditions. We did not develop a questionnaire from scratch but used questions from existing glaucoma-related questionnaires (GQL and GSS; Nelson et al. 1999; Lee et al. 1998) and the NEI-VFQ25 (Massof & Fletcher 2001; Nassiri et al. 2013) and extended them to the different luminance conditions. The development followed the six constructive guidelines of de Vet et al., including a pretest in 13 healthy subjects and two glaucoma patients using the Three-Step Test-Interview (Hak et al. 2008; de Vet et al. 2011). In short, this method implies that (Step 1) respondents were asked to think aloud, and their behaviour was observed while filling in the questionnaire (hesitation, skipping questions, corrections of the chosen response category, etc.). After that (Step 2), we interviewed the respondents to clarify the observations (e.g., 'You stopped for a while, why?'). Finally (Step 3), we asked for experiences and opinions. Here, we also explicitly asked to describe the situations they imagined while filling in the specific questions.

The questionnaire included 15 luminance-specific questions addressing visual performance under five different conditions: (i) presumed optimal luminance (outdoor on a cloudy day, four questions), (ii) low luminance (outdoor at night, three questions), (iii) high luminance (outdoor on a sunny day, four questions), (iv) sudden decrease in luminance (two questions) and (v) sudden increase (two questions). Within the questionnaire, the questions were ordered by activity (e.g. seeing, walking/cycling, driving), starting with the question regarding the high luminance condition, then optimal, low and ending with questions regarding the changing luminance conditions. The questionnaire was developed in Dutch.

### Data analysis

Glaucoma patients and controls had a different age distribution. To enable a fair comparison between the groups, we equalized the number of patients and controls per age bin of 10 years, by applying a weight factor. For example, if in a certain age bin there were twice as many controls as cases, the controls were entered in the analysis with a weight factor of 0.5. Similarly, if there were more patients than controls in a certain age bin, the patients were entered with a weight factor <1. In this way, the effective number of subjects decreased slightly, but the weighted subjects formed age-matched groups.

Questions regarding visual complaints contained five response options. For the initial descriptive analysis, we dichotomized these response options into 'No complaints' and 'Complaints'.

The answer options 'No difficulty at all' and 'A little difficulty' became 'No complaints'; 'A lot of difficulty', 'Extreme difficulty' and 'Stopped doing this because of my eyesight' became 'Complaints'. Every question also had an answer option 'Not applicable', which we considered as missing during analysis. We calculated, per question, the percentage of complaints within the group of glaucoma patients and controls, and the corresponding difference with 95% confidence interval (CI). We compared the percentage of complaints between the groups with chi-squared tests with Bonferroni's correction. We considered the difference between the groups as clinically relevant if the difference was both statistically significant and at least 10%. Similarly, if this difference was at least 10% larger under extreme luminance conditions compared to the difference with optimal luminance, we considered the complaints of glaucoma patients as disproportionately more pronounced under extreme luminance conditions. The value of 10% is to a certain extent arbitrary, but prevents emphasize on small differences that may be statistically significant, but not clinically relevant. We used a chi-squared test for trend with Bonferroni's correction to determine whether complaints were more frequent with increasing disease severity within the group of glaucoma patients.

Not all tasks (e.g. reading) can be performed under all luminance conditions. To enable a fair comparison between all luminance conditions, we selected, for each luminance condition, one question that did not refer to a specific task, that is, seeing or adapting. For those luminance conditions with more than one 'task-independent' question available, we chose the question that differentiated best between glaucoma patients and controls.

To determine whether complaints from the four extreme luminance conditions (low, high, sudden decrease, sudden increase) were associated, we used the selected task-independent questions (see above), made $2 \times 2$ tables, and calculated Phi coefficients for each combination of conditions, for the glaucoma patients. Differences between the conditions were evaluated with McNemar's test with continuity correction.

We considered a p value of 0.05 or less statistically significant. Bonferroni's correction was applied if applicable.

# Results

We retrieved 178 questionnaires from 221 glaucoma patients (response rate 81%) and 182 questionnaires from controls. The mean [standard deviation (SD)] age of the glaucoma patients was 72.2 (10.0) years and of the controls 65.7 (10.8) years. After weighting, both groups had a size of 135 subjects, with a mean (SD) age of 69.6 (9.3) years for the glaucoma patients and 69.0 (9.3) years for the controls ($p = 0.63$). The glaucoma patients consisted of fewer females compared to the controls (47% versus 64%; $p = 0.01$). Most of the patients had early glaucoma (62%); about one-third had either moderate (16%) or severe (22%) glaucoma in the better eye. The median (IQR) HFA MD of the better eye was −4.5 (−10.7 to −1.9) dB. Most of the glaucoma patients (80%) had a pretreatment intraocular pressure of 21 mmHg or more.

Figure 1 shows two examples of responses to the questions 'Seeing outside on a cloudy day' (left panel) and 'Seeing outside at night when there is no moonlight' (right panel). The upper row presents all response options for controls and patients; the lower row presents the dichotomized responses for controls and patients with increasing disease severity.

Table 1 presents the dichotomized results for the 15 included questions, categorized in five luminance conditions. The table shows the percentages of patients with glaucoma and controls who reported complaints, and the corresponding differences. Within each luminance condition, the questions were ranked according to these differences. All questions resulted in a significant difference between glaucoma patients and controls at a Bonferroni corrected p value of 0.003 (0.05/15), except for 'Walking or cycling on a cloudy day' ($p = 0.01$) and 'Seeing outside on a cloudy day' ($p = 0.02$). Two of four questions regarding the optimal luminance condition resulted in a clinically relevant difference (for definition, see Methods section) between glaucoma patients and controls; all questions regarding the extreme luminance conditions resulted in a clinically relevant difference between glaucoma patients and controls.

Within the group of glaucoma patients, the frequency of complaints increased significantly with increasing disease severity at a Bonferroni-corrected p value of 0.003 (0.05/15) for all luminance-specific questions, except for 'Seeing outside on a cloudy day' ($p = 0.28$) and 'Seeing outside on a sunny day' ($p = 0.005$).

The five task-independent questions were marked in Table 1 with a *. The difference between the groups for these questions under extreme luminance conditions, compared to the optimal luminance condition, was more than 10%. That is, visual complaints of glaucoma patients were, compared to controls, disproportionately more pronounced under extreme luminance conditions.

Figure 2 shows the difference in complaints between glaucoma patients and controls for the five task-independent questions, stratified by gender. The most obvious difference in the difference between glaucoma patients and controls was found between the optimal luminance condition and the low luminance condition, for both genders. Generally, the differences were more pronounced in women than in men. Male and female glaucoma patients had similar MD values of the better eye ($p = 0.26$, Mann–Whitney *U*-test).

Table 2 presents the $2 \times 2$ tables and corresponding Phi coefficients describing the association between the selected task-independent questions belonging to the four extreme luminance conditions, for the glaucoma patients. All Phi coefficients were significant at a Bonferroni-corrected p value of 0.008 (0.05/6); they varied between 0.40 and 0.62. McNemar's test showed a significant difference at a Bonferroni-corrected p value of 0.008 (0.05/6) for low versus high, low versus sudden decrease and low versus sudden increase (all $p < 0.001$), uncovering the low luminance condition as the most difficult condition for glaucoma patients.

# Discussion

Differences in visual complaints between glaucoma patients and controls are small with optimal luminance but quite pronounced under extreme luminance conditions. The low luminance condition discriminates best, and

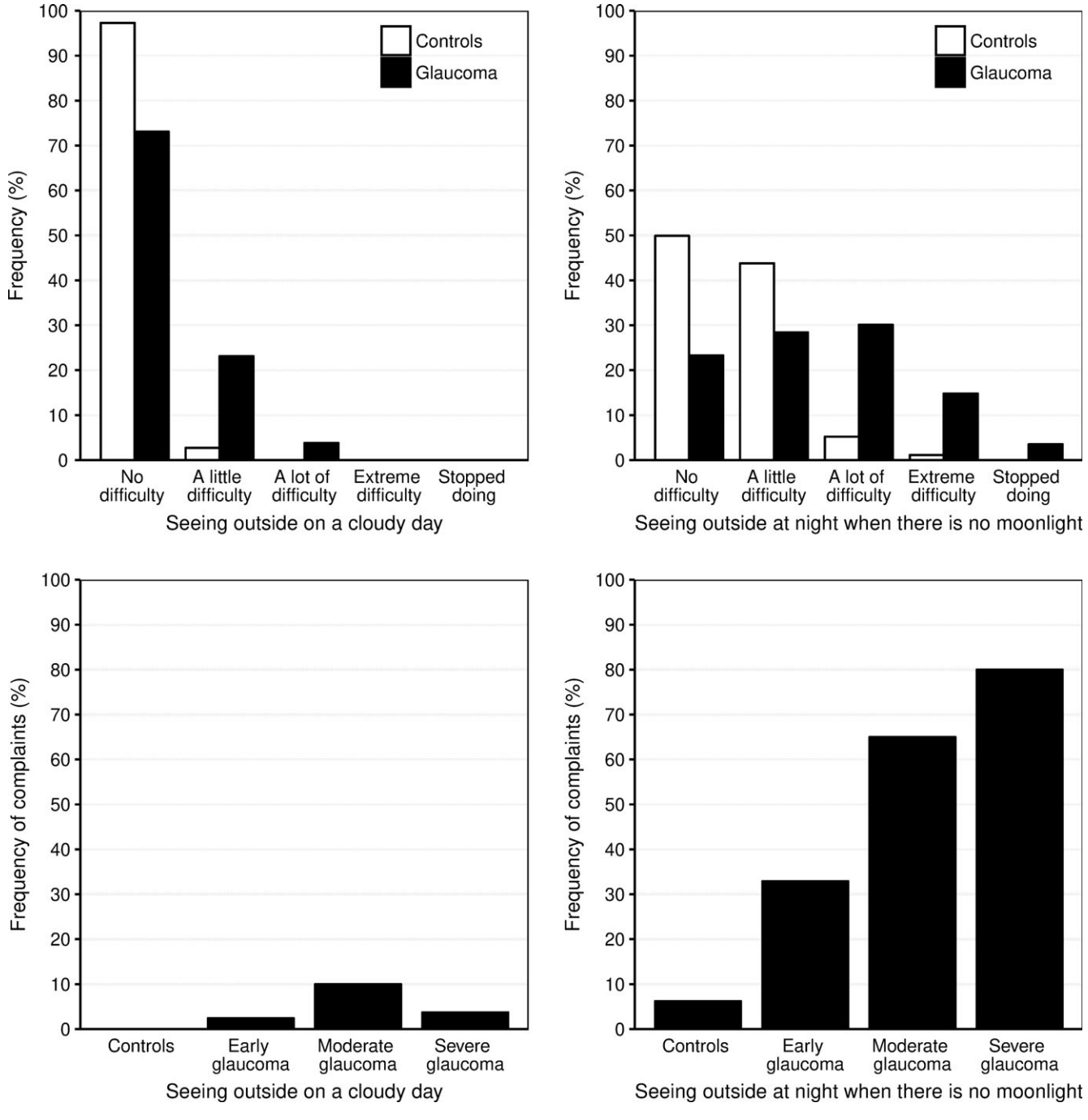


**Fig. 1.** Examples of responses to the questions. Left panel: 'Seeing outside on a cloudy day'; right panel: 'Seeing outside at night when there is no moonlight'. Upper row: all response options for controls and glaucoma patients; lower row: dichotomized responses for controls and glaucoma patients with increasing disease severity.

complaints are more frequent with increasing disease severity.

Earlier vision-specific questionnaires included some questions related to light, dark or adaptation, but did not analyse them separately (e.g. Mangione et al. 2001). Studies that used questionnaires with light, dark or adaptation subscales revealed that glaucoma patients do indicate that they experience difficulty under extreme luminance conditions, which is in agreement with our findings (Sherwood et al. 1998; Nelson et al. 2003; Wren et al. 2009; Prior et al. 2013). One study showed an association with the severity of the visual field and the answers to a question on dark adaptation (Viswanathan et al. 1999). Other studies reported frequencies of complaints in patients, without comparing with controls. Hu et al. (2014) found, in glaucoma patients, complaint frequencies of 57% for the low and 42% for the high luminance condition. We found 48% for the question 'Seeing outside at night when there is no moonlight' and 22% for the question 'Seeing outside on a sunny day'. Nelson et al. (1999) found that 54% of glaucoma patients complained about adaptation to different levels of lighting. Janz et al. (2001a) researched symptoms in newly diagnosed glaucoma patients and found complaint frequencies of 30%, 42% and 41% for the low, high and decreasing luminance condition, respectively. Lee

**Table 1.** Percentages of glaucoma patients and controls who reported complaints, per question; questions were ranked, per category, according to the differences between glaucoma patients and controls.

| Questions ordered by luminance condition. All questions were preceded by 'Because of your eyesight, how much difficulty do you have with...' If applicable, subjects were asked to answer the questions as if they were wearing their glasses or contact lenses | Complaints (%) | | | Missing (%) |
|---|---|---|---|---|
| | Glaucoma | Controls | Difference (95% confidence interval) | Glaucoma versus controls |
| Presumed optimal luminance | | | | |
| Driving on a cloudy day | 14.4 | 0 | 14.4 (7.6–21.3) | 23.0/14.8 |
| Reading outside on a cloudy day | 11.4 | 0 | 11.4 (5.8–17.0) | 5.9/3.0 |
| Walking or cycling on a cloudy day | 4.3 | 0 | 4.3 (0.8–7.9) | 5.9/2.2 |
| Seeing outside on a cloudy day* | 3.8 | 0 | 3.8 (0.5–7.1) | 3.7/1.5 |
| Low luminance | | | | |
| Seeing outside at night when there is no moonlight* | 48.4 | 6.3 | 42.1 (32.1–51.9) | 9.6/3.7 |
| Walking or cycling at night on an unlit country road | 53.6 | 13.7 | 39.9 (28.7–51.2) | 16.3/14.1 |
| Driving at night on an unlit country road | 49.7 | 12.7 | 37.0 (25.2–48.9) | 26.7/20.7 |
| High luminance | | | | |
| Reading outside in the sun | 34.3 | 3.9 | 30.4 (21.5–39.4) | 5.2/2.2 |
| Seeing outside on a sunny day* | 22.2 | 1.3 | 20.9 (13.-28.3) | 2.2/1.4 |
| Walking or cycling on a sunny day | 18.7 | 0.6 | 18.1 (11.2–25.1) | 5.2/2.2 |
| Driving on a sunny day | 20.2 | 1.7 | 18.5 (10.2–26.8) | 25.9/17.0 |
| Sudden decrease in luminance | | | | |
| Adapting to dim lights, when coming from a well-lit environment* | 32.4 | 0.8 | 31.6 (23.3–39.9) | 3.7/3.0 |
| Adapting to less light, when coming from the bright sunlight | 24.9 | 1.3 | 23.6 (15.8–31.4) | 4.4/3.0 |
| Sudden increase in luminance | | | | |
| Adapting to bright sunlight, when coming from less light* | 25.0 | 2.7 | 22.3 (14.3–30.3) | 3.7/3.7 |
| Adapting to a well-lit environment, when coming from dim lights | 13.0 | 0.8 | 12.2 (6.2–18.3) | 3.7/3.0 |

*Selected task-independent question (see Methods section).

et al. (1998) found high complaint frequencies for the low (82%) and high (46%) luminance condition. They also included controls and found that complaints regarding the low and high luminance condition discriminated best between patients and controls, compared to other (non-luminance-specific) symptoms. Tatemichi et al. (2012), who used the same questions as Lee et al. but focussed on normal tension glaucoma patients, found somewhat lower complaint frequencies for the low (50%) and high (12%) luminance condition. Again, the low luminance condition discriminated best between patients and controls. To summarize, the general message from these studies and our data is that a large percentage of glaucoma patients report difficulties with their visual functioning under extreme luminance conditions. An exception seems to be a study by Iester & Zingirian (2002), in which glaucoma patient complaint frequencies of 10 and 14% were reported for the high and decreasing luminance condition, respectively. None of the earlier studies reported complaint frequencies for the optimal and increasing luminance condition.

A limitation of this study is that the glaucoma patients and controls differed significantly regarding age and gender. This resulted from the fact that we invited primarily the spouses of the patients as controls. We invited the spouses because (i) they live under the same luminance conditions as the corresponding cases and (ii) we assumed them to be of similar age. However, spouses may differ in age, and because glaucoma is an age-related disease, the elder of the two is more likely to be the glaucoma case. Using a weight factor, we normalized the age distribution of the control group to the glaucoma group. There were more women in the control group (because the elder of the two is more likely to be the male) than in the group of glaucoma patients and women reported more complaints than men, a finding that is consistent with other studies reporting that women generally have a more pronounced illness

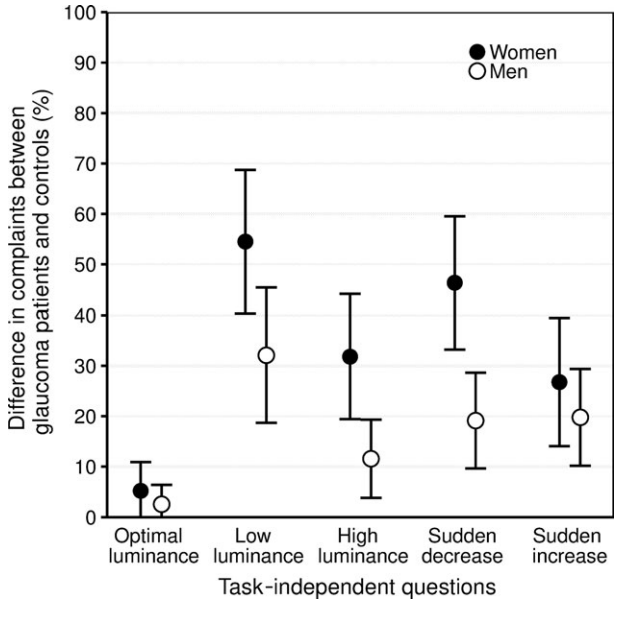


**Fig. 2.** Differences in complaints between glaucoma patients and controls for the five selected task-independent questions, stratified by gender. Error bars denote 95% confidence intervals.

**Table 2.** 2 × 2 tables showing the answers of the glaucoma patients to the task-independent questions (marked with a * in Table 1) for the four extreme luminance conditions.

| | High luminance | | |
|---|---|---|---|
| | No complaints | Complaints | Phi |
| Low luminance | | | |
| No complaints | 58 | 4 | 0.40 |
| Complaints | 35 | 23 | |
| | Sudden decrease | | |
| | No complaints | Complaints | Phi |
| Low luminance | | | |
| No complaints | 54 | 6 | 0.46 |
| Complaints | 28 | 31 | |
| | Sudden increase | | |
| | No complaints | Complaints | Phi |
| Low luminance | | | |
| No complaints | 55 | 5 | 0.40 |
| Complaints | 33 | 25 | |
| | Sudden decrease | | |
| | No complaints | Complaints | Phi |
| High luminance | | | |
| No complaints | 79 | 20 | 0.50 |
| Complaints | 7 | 22 | |
| | Sudden increase | | |
| | No complaints | Complaints | Phi |
| High luminance | | | |
| No complaints | 88 | 11 | 0.61 |
| Complaints | 7 | 21 | |
| | Sudden increase | | |
| | No complaints | Complaints | Phi |
| Sudden decrease | | | |
| No complaints | 82 | 6 | 0.62 |
| Complaints | 15 | 27 | |

perception than men (Verbrugge 1980; Wingard 1984; Janz et al. 2001a). The gender imbalance might have resulted in an underestimation of the observed luminance-specific differences. Another limitation is that the cases knew their diagnosis, and the controls presumably presumed that they were healthy. This limitation is not specific to our study; it will affect any case–control study with a questionnaire or other subjective test involved. Patients may exaggerate their impairments or they may become used to them. The latter option seems to be more common in glaucoma, but we can only speculate if that is also the case for luminance-specific impairments. Importantly, (i) the percentages of complaints were very low for questions that addressed the optimal luminance condition and (ii) we found a clear dose–response relationship for the extreme luminance conditions. Both findings indicate the existence of some real luminance-specific effects. We did not screen for the presence of other eye diseases but rather assumed that they would be equally distributed amongst the groups. In this way, we aimed for a realistic sample of elderly rather than super normals. Generally, missing values were more frequent in glaucoma patients than in controls (last column of Table 1). If we assume that this is due to mixing up 'Stopped doing this because of my eyesight' and 'Not applicable' by the patients, then the differences between glaucoma patients and controls have been underestimated (we considered 'Not applicable' as missing values during analysis). The high percentages of missing values for driving-related questions suggest that this mixing up is indeed the case. Strengths of our study are the sample size, the inclusion of questions regarding all five different luminance conditions and the presence of a control group.

Currently, the primary functional test in glaucoma, perimetry, is performed at a comfortable, moderate background luminance of 10 cd/m$^2$. Our results suggest that a much better discrimination between glaucoma and healthy might be obtained by performing this test at a lower background luminance. Performing perimetry in glaucoma patients and controls over a wide range of luminances could be a good starting point for future research; earlier studies addressing perimetry as a function of luminance included healthy subjects only (Klewin & Radius 1986; Heuer et al. 1989; Membrey et al. 1999).

Reported complaint frequencies in response to the question ′Seeing outside at night when there is no moonlight′ correspond to a sensitivity of 48% at a specificity of 94%, and a sensitivity of 33% and 74% for early and moderate/severe glaucoma, respectively. This suggests some potential for questionnaires in the field of glaucoma screening. Obviously, this potential has to be confirmed in other studies, especially in studies where the cases are not aware of their diagnosis. Screening with questionnaires may be interesting for research purpose, for example, for case finding in huge cohort studies, where a full eye examination in all participants is not easily realized (Kiefer et al. 2013).

In conclusion, the common view of glaucoma as a disease that is asymptomatic, especially in an early stage, appears only valid with optimal luminance. Differences in visual complaints between glaucoma patients and controls are greater under extreme luminance conditions, especially in the dark. This offers opportunities for better diagnostic tests and may be even screening. As the complaints impact vision already in an early disease stage, this study indirectly supports a timely detection and treatment of glaucoma.

# References


Bengtsson B & Heijl A (2000): False-negative responses in glaucoma perimetry: indicators of patient performance or test reliability? Invest Ophthalmol Vis Sci **41**: 2201–2204.

Duke-Elder S (1969): System of ophthalmology: diseases of the lens and vitreous; glaucoma and hypotony. St. Louis, MO: CV Mosby 443–477.

Freeman EE, Muñoz B, West SK, Jampel HD & Friedman DS (2008): Glaucoma and quality of life: the Salisbury eye evaluation. Ophthalmology **115**: 233–238.

van Gestel A, Webers CAB, van Beckers HJM, Dongen MCJM, Severens JL, Hendrikse F & Schouten JSAG (2010): The relationship between visual field loss in glaucoma and health-related quality-of-life. Eye **24**: 1759–1769.

Gutierrez P, Wilson MR, Johnson C et al. (1997): Influence of glaucomatous visual field loss on health-related quality of life. Arch Ophthalmol **115**: 777–784.

Hak T, Van der Veer K & Jansen H (2008): The three-step test-interview (TSTI): an observation-based method for pretesting self-completion questionnaires. Surv Res Methods **2**: 143–150.

Heeg GP, Blanksma LJ, Hardus PLLJ & Jansonius NM (2005): The Groningen longitudinal glaucoma study. I. Baseline sensitivity and specificity of the frequency doubling perimeter and the GDx nerve fibre analyser. Acta Ophthalmol Scand **83**: 46–52.

Heuer DK, Anderson DR, Feuer WJ & Gressel MG (1989): The influence of decreased retinal illumination on automated perimetric threshold measurements. Am J Ophthalmol **108**: 643–650.

Hu CX, Zangalli C, Hsieh M, Gupta L, Williams AL, Richman J & Spaeth GL (2014): What do patients with glaucoma see? Visual symptoms reported by patients with glaucoma Am J Med Sci **348**: 403–409.

Iester M & Zingirian M (2002): Quality of life in patients with early, moderate and advanced glaucoma. Eye **16**: 44–49.

Janz NK, Wren PA, Lichter PR, Musch DC, Gillespie BW & Guire KE (2001a): Quality of life in newly diagnosed glaucoma patients: the Collaborative Initial Glaucoma Treatment Study. Ophthalmology **108**: 887–898.

Janz NK, Wren PA, Lichter PR, Musch DC, Gillespie BW, Guire KE, Mills RP; CIGTS Study Group (2001b): The Collaborative Initial Glaucoma Treatment Study Interim quality of life findings after initial medical or surgical treatment of glaucoma. Ophthalmology **108**: 1954–1965.

Junoy Montolio FG, Meems W, Janssens MSA, Stam L & Jansonius NM (2016): Lateral inhibition in the human visual system in patients with glaucoma and healthy subjects: a case-control study. PLoS ONE **11**: e0151006.

Katz J, Sommer A, Gaasterland DE & Anderson DR (1991): Comparison of analytic algorithms for detecting glaucomatous visual field loss. Arch Ophthalmol **109**: 1684–1689.

Kiefer AK, Tung JY, Do CB, Hinds DA, Mountain JL, Francke U & Eriksson N (2013): Genome-wide analysis points to roles for extracellular matrix remodeling, the visual cycle, and neuronal development in myopia. PLoS Genet **9**: e1003299.

Klewin KM & Radius RL (1986): Background illumination and automated perimetry. Arch Ophthalmol **104**: 395–397.

Kulkarni KM, Mayer JR, Lorenzana LL, Myers JS & Spaeth GL (2012): Visual field staging systems in glaucoma and the activities of daily living. Am J Ophthalmol **154**: 445–451.

Lee BL, Gutierrez P, Gordon M, Wilson MR, Cioffi GA, Ritch R, Sherwood M & Mangione CM (1998): The Glaucoma Symptom Scale. A brief index of glaucoma-specific symptoms. Arch Ophthalmol **116**: 861–866.

Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S & Hays RD (2001): Development of the 25-list-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol **119**: 1050–1058.

Massof RW & Fletcher DC (2001): Evaluation of the NEI visual functioning questionnaire as an interval measure of visual ability in low vision. Vision Res **41**: 397–413.

Membrey L, Kogure S & Fitzke FW (1999): A comparison of the effects of neutral density filters and diffusing filters on motion perimetry, white on white perimetry and frequency doubling perimetry. In: Wall M & Wild JM (eds.). Perimetry update 1998/1999. The Hague, the Netherland: Kugler Publications 75–83.

Mills RP, Janz NK, Wren PA & Guire KE (2001): Correlation of visual field with quality-of-life measures at diagnosis in the Collaborative Initial Glaucoma Treatment Study (CIGTS). J Glaucoma **10**: 192–198.

Montolio FG, Wesselink C, Gordijn M & Jansonius NM (2012): Factors that influence standard automated perimetry test results in glaucoma: test reliability, technician experience, time of day, and season. Invest Ophthalmol Vis Sci **53**: 7010–7017.

Nassiri N, Mehravaran S, Nouri-Mahdavi K & Coleman AL (2013): National eye institute visual function questionnaire: usefulness in Glaucoma. Optom Vis Sci **90**: 745–753.

Nelson P, Aspinall P & O'Brien C (1999): Patients' perception of visual impairment in glaucoma: a pilot study. Br J Ophthalmol **83**: 546–552.

Nelson P, Aspinall P, Papasouliotis O, Worton B & O'Brien C (2003): Quality of life in glaucoma and its relationship with visual function. J Glaucoma **12**: 139–150.

Peters D, Heijl A, Brenner L & Bengtsson B (2015): Visual impairment and vision-related quality of life in the Early Manifest Glaucoma Trial after 20 years of follow-up. Acta Ophthalmol **93**: 745–752.

Prior M, Ramsay CR, Burr JM, Campbell SE, Jenkinson DJ, Asoaka R & Francis JJ (2013): Theoretical and empirical dimensions of the Aberdeen Glaucoma Questionnaire: a cross sectional survey and principal component analysis. BMC Ophthalmol **13**: 72.

Sherwood MB, Garcia-Siekavizza A, Meltzer MI, Hebert A, Burns AF & McGorray S (1998): Glaucoma's impact on quality of life and its relation to clinical indicators. A pilot study. Ophthalmology **105**: 561–566.

Tatemichi M, Nakano T, Hayashi T et al. (2012): Symptoms related to glaucomatous visual field abnormalities among male Japanese workers in a population-based setting. Acta Ophthalmol **90**: 546–551.

Verbrugge LM (1980): Sex differences in complaints and diagnoses. J Behav Med **3**: 327–355.

de Vet HCW, Terwee CB, Mokkink LB & Knol DL (2011): Measurement in medicine: a practical guide. Amsterdam, the Netherland: Cambridge University Press 30–65.

Viswanathan AC, McNaught AI, Poinoosawmy D, Fontana L, Crabb DP, Fitzke FW & Hitchings RA (1999): Severity and stability of glaucoma: patient perception compared with objective measurement. Arch Ophthalmol **117**: 450–454.

Wingard DL (1984): The sex differential in morbidity, mortality, and lifestyle. Annu Rev Public Health **5**: 433–458.

Wolfs RC, Borger PH, Ramrattan RS, Klaver CC, Hulsman CA, Hofman A & de Jong PT (2000): Changing views on open-angle glaucoma: definitions and prevalences—The Rotterdam Study. Invest Ophthalmol Vis Sci **41**: 3309–3321.

Wren PA, Musch DC, Janz NK, Niziol LM, Guire KE & Gillespie BW (2009): Contrasting the use of 2 vision-specific quality of life questionnaires in subjects with open-angle glaucoma. J Glaucoma **18**: 403–411.


Received on June 13th, 2017.
Accepted on December 9th, 2017.

*Correspondence*:
Nomdo M. Jansonius
Department of Ophthalmology
University Medical Center Groningen
P.O.Box 30.001
9700 RB Groningen
the Netherlands
Tel: +31 50 3612510
Fax: +31 50 3611709
Email: n.m.jansonius@umcg.nl