Published in final edited form as:

J Glaucoma. 2016 March ; 25(3): e220–e228. doi:10.1097/IJG.0000000000000304.

Ophthalmic and Glaucoma Treatment Characteristics Associated with Changes in Health-Related Quality of Life Before and After Newly Diagnosed Primary Open-Angle Glaucoma in Nurses Health Study Participants

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Abstract

Purpose—To identify attributes related to glaucoma diagnosis or early glaucoma treatment patterns that are associated with changes in health-related quality of life among those with newly diagnosed primary open-angle glaucoma.

Methods—Among Nurses' Health Study participants with incident medical record-confirmed primary open-angle glaucoma diagnosed in 1992–2000, we included 317 women who completed the Short-Form 36 Health Survey pre- and post-diagnosis. The two primary outcomes were 4-year changes (1992–1996 or 1996–2000) in the physical and mental component summary scores. Multiple regression models were used to estimate differences in score changes by early treatment pattern history and characteristics as of diagnosis (i.e., number of eyes affected, history of cataract, macular degeneration, cup-to-disc ratio, intraocular pressure, visual field loss type).

Results—In multivariable models, no ophthalmologic characteristics were associated with physical component score change. However, compared to treatment with eye drops or pills only, laser trabeculoplasty treatment (concomitant with history of treatment with eye drops or pills in 84%) was associated with a worse mental component score change over four years (–2.5 units; 95% confidence interval: –4.6, –0.3); this association was stronger with a family history of glaucoma (p-interaction=0.04) or with bilateral disease (p-interaction=0.001).

Conclusions—Among patients with incident glaucoma, no major factors were associated with change in physical well-being. However, compared to medical treatment only, a history of laser trabeculoplasty, which was commonly accompanied with a history of medical treatment and likely

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None of the authors have conflicts of interest, including financial interests, activities, relationships and affiliations.

represented the need for a second line of treatment, was associated with a worse decline in mental well-being.

Keywords

Quality of life; primary open-angle glaucoma; laser trabeculoplasty; cohort study

INTRODUCTION

Glaucoma is the second leading cause of blindness worldwide – in 2020, an estimated 58.6 million will have a diagnosis of primary open-angle glaucoma (POAG), and 11.1 million people will be bilaterally blind from POAG.¹ Because early glaucoma is by nature asymptomatic, a majority of people with the disease are undiagnosed, and thus there is likely an even greater burden of disease than can be estimated based on numbers of current patients. In addition to the financial burden of treatment, glaucoma affects patients' daily functioning, particularly the ability to ambulate and operate a motor vehicle,² and it is associated with psychological distress.³

Previous research examining health-related quality of life (HRQoL) in glaucoma has focused on patients with pre-existing disease. For example, among those with prevalent POAG, studies have reported that greater visual field loss^{4–13} was associated with worse HRQoL, while studies of the effect of different glaucoma treatments^{14,15} (e.g., medical vs. surgical treatment) have shown conflicting results. In the few studies among patients with newly-diagnosed POAG, there have been reports of an increased fear of blindness¹⁶ and increased depression and anxiety¹⁷ related to patients' self-reported deficiencies in visual function that did not necessarily correlate with clinical measures of visual field defects. Thus, given the potential impact of a glaucoma diagnosis and the related treatments on HRQoL, particularly on mental health measures, a better understanding of such changes in a population-based sample of incident POAG patients may be clinically informative.

To our knowledge, no prior study has examined change in HRQoL before and after a glaucoma diagnosis. This study evaluated 317 women who were participants of the Nurses' Health Study and were newly diagnosed with POAG between 1992 and 2000. The goal of the study was to identify glaucoma-related patient characteristics as of diagnosis and early treatment patterns that were associated with HRQoL changes before and after receiving a glaucoma diagnosis.

METHODS

Study Population

The NHS was initiated in 1976 when 121 700 registered female nurses, aged 30 to 55 years, completed a mailed baseline questionnaire about lifestyle and medical history. Follow-up questionnaires were sent by mail and administered biennially to update information on diet, medication, lifestyle and newly diagnosed diseases, such as glaucoma. The follow-up rate has been >90% of total potential person-years.

We first assessed HRQoL with the Medical Outcomes Short Form-36 Health Survey (SF-36) version 1¹⁸ on the 1992 questionnaire and administered the SF-36 again in the 1996 and 2000 questionnaires. Among the NHS participants, those who completed a 1980 food frequency questionnaire, were free of cancer, were actively participating in the study and were free of prevalent glaucoma was the risk population, and incident glaucoma cases were identified from this group. In the current analysis, we identified 443 participants whose date of POAG diagnosis occurred between 1992 and 1996 or between 1996 and 2000, to evaluate change in HRQoL before and after diagnosis over a 4-year period. We excluded 126 participants who had incident POAG in the same period but had incomplete pre- and post-diagnosis SF-36 data; thus, we included 317 remaining participants in the current analysis. Compared to the 317 participants included in the analysis, the 126 excluded participants were similar in all covariates listed in the later “Covariates” section, except that the excluded participants were significantly less likely to have paracentral glaucoma than the included participants ($p=0.004$; 1.6% versus 9.6%) and were more likely to be married ($p=0.02$; 23.8% versus 14.5%). Excluded participants had a nominal, nonsignificant higher rate of myocardial infarction ($p=0.21$; 4.0% vs. 1.9%). They also had slightly more advanced glaucoma at diagnosis with higher frequencies of having both eyes affected ($p=0.94$; 37.3% vs. 36.9%) and of having both paracentral and peripheral visual field (VF) loss ($p=0.29$; 38.1% vs. 32.8%), but none of these differences were significant. The Institutional Review Boards of Brigham and Women’s Hospital and Harvard School of Public Health approved this study.

POAG case ascertainment

From participants with a self-report of glaucoma on the biennial questionnaires, we requested permission to retrieve medical information, and we contacted the diagnosing eye care provider to request that a glaucoma questionnaire be completed. This questionnaire asked about maximum IOP, optic nerve features, status of the filtration apparatus and presence of exfoliation material or other secondary causes for elevated IOP. In lieu of completing the questionnaire, eye care providers could send the complete medical records. We also requested all visual field reports supporting the glaucoma diagnosis. A glaucoma specialist (LRP) reviewed all medical records to confirm POAG cases according to standardized criteria. Only those appraised as either “definite” or “probable” POAG were included as cases in this analysis. For definite POAG cases, we required that: (1) gonioscopy showed that angles were not occludable in either eye, (2) slit lamp biomicroscopy showed no indication in either eye of pigment dispersion syndrome, uveitis, exfoliation syndrome, trauma, or rubeosis, and (3) reproducible visual field (VF) defects were present and consistent with glaucoma (peripheral VF loss including nasal step, nasal depression, or temporal wedge defects or paracentral scotoma). For all VF defects, we required that the defect be present on at least 2 reliable tests. There was no requirement for the type of perimetry performed; however, in 95% of cases, static full threshold testing was documented and only in <1% kinetic visual fields were used. For static threshold or suprathreshold testing, we considered the field reliable if the fixation loss rate was $\leq 33\%$, the false positive rate was $\leq 20\%$ and the false negative rate was $\leq 20\%$. For kinetic visual fields, we consider the field reliable unless there was notation by the examiner to the contrary. For probable POAG cases, the same slit lamp exam and VFs criteria were also required, but for

determining the angle of the anterior chamber, documentation of pupil dilation without subsequent adverse events was accepted in lieu of gonioscopy. The date of diagnosis was based on the earliest date of any of the following glaucomatous signs: intraocular pressure 22 mmHg, cup to disc ratio 0.6, glaucomatous VF loss (where the specific VF defect is reproduced on a later reliable VF test).

SF-36 data

The SF-36 questions included in the follow-up questionnaires assessed 8 domains of HRQoL,¹⁸ that can be broadly categorized into four “physical dimensions” (general health perceptions, bodily pain, physical functioning and role limitations due to physical health problems) and four “mental dimensions” (mental health, role limitations due to emotional problems, vitality and social functioning). Each domain was scored from 0 to 100, with higher scores reflecting better HRQoL.

There were two primary outcomes of this study: the physical component score (PCS), and mental component score (MCS). These are component summary scores that reflect the overall physical and mental health dimensions based on the eight subscale scores. The individual scores were first converted into z-scores, using pre-established means and standard deviations from the general US population norms,¹⁸ and transformed such that the mean score for each of the 8 subscales was 50 (with a standard deviation [SD] of 10), to help interpret the data across the various scores by having a “built-in” reference. The two summary scores were constructed by summing these component scores using a weighted average where the weights were derived from a principle components analysis.^{18,19} The instrument has been extensively validated,^{20,21,22,23} has good construct validity,^{22,23} and high test-retest reliability²¹ and internal consistency.^{21,22,23}

Covariates

In follow-up biennial questionnaires, we obtained updated information on demographics, lifestyle, health and other characteristics that were included as covariates in multivariable analyses: age, highest attained education level, husband’s highest attained education level, marital status, living arrangement, body mass index, cigarette smoking, physical activity, age at menopause, postmenopausal hormone use, self-reported history of physician-diagnosed comorbid conditions (hypertension, diabetes, hypercholesterolemia, myocardial infarction, osteoarthritis or rheumatoid arthritis, chronic respiratory conditions [asthma, emphysema or chronic bronchitis], depression, cataract extraction or cataract diagnosis, age-related macular degeneration [AMD]) and family history of glaucoma. From the medical records dating back to the date of glaucoma diagnosis, we obtained the following information: cup to disc ratio, maximum untreated intraocular pressure (IOP) across affected eyes, number of eyes showing glaucomatous VF loss, type of VF loss (peripheral VF loss only, paracentral scotoma only or peripheral VF loss and paracentral scotoma) and type of treatment (eye drops or pills only, laser trabeculoplasty, trabeculectomy) (in this study, no participants underwent alternative forms of glaucoma filtration surgery such as glaucoma drainage device implantation).

Statistical Analysis

For those diagnosed between 1992 and 1996, we used variables assessed as of the 1992 questionnaire and the ophthalmological characteristics/history from the date of diagnosis (or as of confirmation for glaucoma treatment history) to predict change in the PCS and MCS scores from 1992 to 1996. For those diagnosed between 1996 and 2000, we used corresponding variables as of 1996 and at diagnosis to predict change in the PCS and MCS scores from 1996 to 2000. For the glaucoma treatment history variables, because some participants had laser trabeculoplasty or trabeculectomy after the post-diagnosis HRQoL questionnaire, we conducted sensitivity analyses where we excluded such participants.

We first performed univariate analyses of PCS and MCS changes by 8 variables of interest: history of cataract extraction or cataract diagnosis, age-related macular degeneration, family history of glaucoma, cup to disc ratio (i.e., whether 0.6 or not), maximum untreated IOP across affected eyes (i.e., whether 22 mmHg or not), number of eyes showing glaucomatous VF loss, type of VF loss (peripheral VF loss only, paracentral scotoma only or peripheral VF loss and paracentral scotoma) and type of treatment to date (eye drops or pills only; laser trabeculoplasty [may also have had eye drops or pills but not treated with trabeculectomy]; trabeculectomy [may also have had eye drops or pills or laser trabeculoplasty]). Next, we used multiple linear regression models with 4-year change in the PCS and MCS as the outcomes, and we adjusted for pre-diagnosis HRQoL scores, time between the two HRQoL assessments, date of diagnosis, time between pre-diagnosis HRQoL assessment and diagnosis date and the 4-year period (1992–1996 or 1996–2000). Finally, in full multivariable-adjusted models, we additionally adjusted for the covariates listed in the previous “Covariates” section.

We were interested *a priori* in the potential for effect modification by number of eyes affected²⁴ and family history of glaucoma (a characteristic that can affect individual expectations of trajectory of disease). We tested interactions by evaluating the significance of interaction terms of each predictor of interest with the two effect modifiers in multiple linear regression models.

All analyses were performed using SAS software, version 9.2 (SAS Institute, North Carolina). A two-tailed *P* value < 0.05 was considered statistically significant.

RESULTS

Among 317 women with incident POAG, the mean age at diagnosis was 64.0 [$\pm$ 6.4] years, and 45.4% reported a family history of glaucoma (Table 1). Most patients had early glaucomatous loss at diagnosis – 63.1% were affected in one eye, and 57.7% had peripheral visual field loss only. Most patients were on eye drops or pills only (65.3%), while 16.1% were treated with laser trabeculoplasty, with or without drops or pills but without trabeculectomy. Finally 6.3% of patients underwent trabeculectomy with or without a history of laser trabeculoplasty, eye drops, or pills,

Among patients with incident POAG, no major ophthalmological characteristics were significantly associated with 4-year change in PCS (Table 2). For example, we observed

non-significant differences in 4-year change between women who had paracentral and peripheral visual field losses (mean PCS_{before diagnosis} = 48.5; mean PCS_{after diagnosis} = 45.3; mean PCS change over 4 years = -3.2) compared to women who had peripheral loss only (mean PCS_{before diagnosis} = 47.8; mean PCS_{after diagnosis} = 46.0; mean PCS change over 4 years = -1.7) (multivariable-adjusted difference in change over 4 years between the two groups = -1.3; 95% confidence interval [CI]: -3.4, 0.9). Also, women with both eyes affected tended to have a slower change in score (mean PCS_{before diagnosis} = 47.2; mean PCS_{after diagnosis} = 45.5; mean PCS change over 4 years = -1.7) compared to women with one eye affected (mean PCS_{before diagnosis} = 48.3; mean PCS_{after diagnosis} = 45.7; mean PCS change over 4 years = -2.6) (multivariable-adjusted difference in change over 4 years between the two groups = 1.4; 95% CI: -0.7, 3.4).

For MCS, comparing women with or without family history or women with both eyes versus only one eye affected did not show significant differences in change over time (Table 2). However, compared to women who reported being treated with eye drops or pills only (mean MCS_{before diagnosis} = 53.3; mean MCS_{after diagnosis} = 55.0; mean MCS change over 4 years = 1.70), women with a history of having received laser trabeculoplasty [with or without eye drops or pills but without trabeculectomy] (mean MCS_{before diagnosis} = 52.8; mean MCS_{after diagnosis} = 50.0; mean MCS change over 4 years = -0.84) was associated with a worse change in the MCS score (multivariable adjusted difference in change over 4 years = -2.5; 95% CI: -4.6, -0.3). This worse decline in MCS with laser trabeculoplasty compared with eye drops or pills only (multivariable adjusted difference in change over 4 years = -2.5; 95% CI: -4.6, -0.3) was comparable to the difference in decline in the MCS score observed between women with depression and women without depression among these same 317 participants (multivariable adjusted difference in change over 4 years for those with depression compared to those without depression = -1.8; 95% CI: -6.1, 2.6). Of the 51 participants who had received trabeculoplasty, 43 also reported use of eye drops or pills; when the analyses were restricted to these 43 women, the association with laser trabeculoplasty was slightly worse in relation to MCS: multivariable adjusted difference in change over 4 years = -3.2 (95% CI: -5.4, -0.9). In alternative sensitivity analyses where we excluded the 23 of the 51 with laser trabeculoplasty who had their procedure after their 2nd post-diagnosis HRQoL, we observed similar adverse associations with MCS: a multivariable adjusted difference in change over 4 years = -2.8 (95% CI: -5.5, -0.1). Trabeculectomy [with or without eye drops or pills or laser trabeculoplasty] was not associated (0.8; 95% CI: -2.4, 4.1) with change in MCS likely due to low power (as only 6.3% had this procedure). In alternative sensitivity analyses where we excluded the 12 of the 20 with trabeculectomy who had their surgery after their 2nd post-diagnosis HRQoL, we observed no significant differences in MCS: a multivariable adjusted difference in change over 4 years = -0.3 (95% CI: -5.2, 4.7).

To evaluate the possibility of reverse causation, where those who are depressed might have poorer adherence to eye drops or pills and were therefore more likely to be prescribed laser trabeculoplasty, we conducted analyses excluding those with depression as of the first HRQoL assessment or excluding those with MCS scores below the median. However, the adverse associations with laser trabeculoplasty and worse change in MCS persisted, although they were non-significant due to lower power (data not shown).

We evaluated whether the worse decline among women who reported history of laser trabeculoplasty compared to women with eye drops or pills only was more apparent in certain subgroups of women. We observed that the adverse association with laser trabeculoplasty compared with eye drops or pills only in relation to 4-year change in MCS was suggestively more apparent in those with a family history of glaucoma (p-interaction=0.04) or in those with both eyes affected (p-interaction=0.001) (Table 3). Interestingly, while the overall change in MCS in women with both eyes affected compared to the change in women with only one eye affected did not differ significantly overall, among women with a family history of glaucoma, we observed that women with both eyes affected had suggestive worse decline in MCS than women with only 1 eye affected (p-interaction=0.02) (Table 3). No effect modification was observed with these characteristics and PCS.

In secondary analyses, we evaluated the predictors of interest in relation to each of the individual eight domains of the SF-36 (Table 4). We observed a significant association between history of cataract and worse decline in the social functioning score (−3.1; 95% CI: −5.3, −0.8) and between maximum untreated IOP <22 mmHg and slower decline in the domain of role limitations due to emotional issues (2.3; 95% CI: 0.2, 4.3). In addition, a history of laser trabeculoplasty compared to eye drops or pills only was consistently adversely associated with worse decline in the four domains that have greatest weight for the MCS, although most of these associations were not significant. Interestingly, compared to having 1 eye only affected, having both eyes affected was associated with slower decline in all eight domains, although the association was significant only in relation to vitality (score change= 2.1; 95% CI: 0.2, 3.9).

DISCUSSION

Overall, this prospective study showed that no major ophthalmological characteristics are associated with change in PCS from pre- to post-diagnosis of POAG. However, a history of laser trabeculoplasty (which was concomitant with a history of eye drops or pills in 84%) compared to treatment with only eye drops or pills was associated with a larger decline in pre- to post-diagnosis MCS change over four years, particularly among those with a family history of glaucoma or with both eyes affected. Because we evaluated numerous glaucoma- and glaucoma treatment-related factors, we cannot rule out that chance might explain these associations and thus, the results should be interpreted with caution.

We speculate that the adverse association of history of laser trabeculoplasty with worse change in MCS is highly unlikely to reflect the notion that laser trabeculoplasty *per se* is causing worse decline in mental well being. Rather, it is possible that some patients who had used pills/eye drops prior to the laser trabeculoplasty had had side effects with eye drops, which may have affected their quality of life.²⁵ More importantly, in 1992–2000, laser trabeculoplasty was a common second line of therapy²⁶ and it followed medical treatment in 84% of NHS participants; thus patients with laser trabeculoplasty may have become more anxious or depressed because they perceived that laser trabeculoplasty was being used because medications had failed, that their disease may be more severe or difficult to control and that there was a greater risk of disability, loss of independence or blindness. It is

possible that those who received laser trabeculoplasty had a faster worsening of visual field loss (which we did not assess longitudinally) as they had higher frequency of predictors of progression; worsening of visual field loss has been found to increase the risk of depression.²⁷ Compared to those who used eye drops or pills only, those who received laser trabeculoplasty had a higher proportion of those with family history of glaucoma (53.3% vs. 41.0%), with both eyes affected (40.6% vs. 37.3%), with high cup-to-disc ratios (68.1% vs. 53.8%), with high-tension glaucoma (81.7% vs. 67.2%) and with advanced VF loss present in both peripheral and paracentral regions (40.8% vs. 31.2%). Although we adjusted for all of these differences simultaneously, this suggests that those with a laser trabeculoplasty history have an overall clinical profile that predisposes them to greater POAG progression, in terms of visual field loss, as of the second HRQoL assessment. Indeed, severity of POAG in terms of severity of visual field loss has been shown in the majority of studies to correlate with decreased quality of life⁴⁻¹³ and higher rates of anxiety and depression.^{3,28} The association with laser trabeculoplasty on HRQoL might have been different if laser was offered as first line treatment.

Because psychological reassurance of those with a new glaucoma diagnosis may attenuate the decline in quality of life associated with the diagnosis,¹⁵ our data could inform future development of preventive interventions among those who need to receive laser trabeculoplasty in addition to eye drops or pills, especially among those who have both eyes affected or a family history of glaucoma. Indeed, benefits of psychologically-oriented strategies have been successfully demonstrated in randomized trials among patients with pre-existing monocular AMD and newly diagnosed neovascular AMD in the second eye.²⁹

One of this study's strengths is its prospective design, which allows for evaluation of change in HRQoL comparing pre- and post-diagnosis measures in individuals with an incident diagnosis of POAG. To our knowledge, no other study has examined the pre- to post-diagnosis change in HRQoL associated with POAG. In examining the literature, there seems to be more change in HRQoL in early-stage glaucoma¹⁴ as well as soon after diagnosis.¹⁶ Therefore, one strength of this study was that because patients received a POAG diagnosis during the four-year period between SF-36 assessments, they were assessed relatively shortly after diagnosis and were more likely to be in the early stages of disease. In addition, the study is population-based and is therefore more representative of a cross-section of patients in the general population. Another strength of this study was that updated information on many covariates was obtained to adjust for in statistical models in order to reduce confounding bias.

One of the limitations of the study was that while the SF-36 is an overall measure of HRQoL, glaucoma-specific visual function-related HRQoL questions were not asked. Some studies examining HRQoL in glaucoma use a disease-specific questionnaire in an attempt to better assess those aspects of HRQoL that are more affected by visual disabilities, such as dark adaptation, disability glare and activities using peripheral vision.^{4,5,30,31} In addition, the sample size was relatively small with 317 participants who had received a confirmed diagnosis of POAG between responses to SF-36 questionnaires, and therefore we may have had too little power to detect true associations with specific factors. Also, because this was an observational study, residual confounding by factors we were unable to adjust for

remains a possibility. Our findings of worse change in MCS with laser trabeculoplasty versus eye drops or pills only cannot be construed as an effect of laser trabeculoplasty *per se* as the majority were also on medications; only randomized trials would be able to address this issue. Moreover, because we evaluated numerous factors in this study, we cannot rule out chance findings and confirmation of our results by other studies would be warranted. This was a study among only women with POAG, and the findings with MCS may not be generalizable to men (e.g. in one study, women with POAG were shown to have a greater decrease in composite scores of the Visual Function Questionnaire compared to men³¹) or to those with glaucoma suspect or other secondary glaucomas. Furthermore, our study participants were mostly Caucasians with medical training and of higher socioeconomic status with better access to healthcare than the general population who were surveyed in 1992–2000. Thus, it is possible that the self-reported HRQoL changes we report may be different compared to a sample from the general population.

In summary, among patients with incident glaucoma, no major factors were associated with change in physical well being. However, compared to medical treatment only, a history of laser trabeculoplasty, which was commonly accompanied with a history of medical treatment and likely represented the need for a second line of treatment, was associated with a worse decline in mental well being.

Acknowledgments

This work was supported by grants UM1 CA186107, R01 EY09611, and R01 EY015473 (LRP) from the National Institutes of Health. The Harvard Glaucoma Center of Excellence and a Harvard Medical School Distinguished Scholar Award (LRP) also supported this work.

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Table 1

Characteristics and SF-36 scores of participants with incident POAG diagnosis (1992 – 2000) as of the biennial questionnaire prior to diagnosis (1992 or 1996), ophthalmologic characteristics as of diagnosis and treatment history (n=317)

Demographic and health characteristics	Ophthalmologic characteristics	Mean SF-36 scores before diagnosis (SD)
Mean age, years (SD)	64.0 (6.4)	Physical Component Score 47.9 (10.2)
Family history of glaucoma, % (n)	45.4 (144)	Mental Component Score 52.9 (8.5)
Highest attained education level: Graduate school, % (n)	8.8 (28)	Physical functioning 82.1 (19.8)
Husband's education level: Graduate school, % (n)	21.8 (69)	Physical role limitations 70.3 (39.2)
Married, % (n)	85.5 (271)	Emotional role limitations 82.8 (30.6)
Living alone, % (n)	14.2 (45)	Vitality/energy/fatigue 62.9 (19.5)
Mean body mass index (kg/m ²)(SD)	25.9 (5.8)	General mental health 78.6 (14.3)
30 pack-years of smoking, % (n)	16.1 (51)	Social functioning 89.3 (19.3)
Cataract diagnosis or surgery, % (n)	18.9 (60)	Bodily pain 70.9 (22.7)
Macular degeneration, % (n)	4.4 (14)	General health perception 77.8 (19.9)
Depression, % (n)	3.8 (12)	
Arthritis (osteo- or rheumatoid-), % (n)	53.6 (170)	
Chronic respiratory condition, % (n)	12.6 (40)	
Hypertension, % (n)	42.6 (135)	
Hyperlipidemia, % (n)	61.2 (194)	
Diabetes, % (n)	8.2 (26)	
Myocardial infarction, % (n)	1.9 (6)	
Age at menopause <45 years, % (n)	8.2 (26)	
Current postmenopausal hormone use, % (n)	39.8 (126)	
Highest quartile of MET-hours/week, % (n) [‡]	24.6 (78)	

Abbreviations: POAG = Primary Open-Angle Glaucoma; SD = Standard Deviation; IOP = Intraocular Pressure; SF-36 = Medical Outcomes Study Short-Form 36 Health Survey

* Laser trabeculoplasty refers to any report of laser trabeculoplasty with or without drops or pills but without any trabeculectomy

[‡] Trabeculectomy refers to any report of trabeculectomy with or without drops or pills or laser trabeculectomy

[‡] MET-hours/week refers to physical activity in measured as metabolic equivalent-hours per week

Table 2

Difference in change over 4 years in the physical and mental component summary scores by pre-diagnosis characteristics, ophthalmological characteristics at diagnosis and treatment history in participants with incident POAG from 1992 – 2000 (n=317)

	Physical Component Summary	Mental Component Summary
Before diagnosis (mean, SD)	47.9 (10.2)	52.9 (8.5)
After diagnosis (mean, SD)	45.6 (10.6)	54.2 (7.4)
	Difference in score change over 4 years (95% Confidence Interval) *	
Family History: No (54.6%, n=173)	0 (REF)	0 (REF)
	Univariate analysis	-1.3 (-3.2, 0.7)
Yes (45.4%, n=144)	Multivariable-adjusted model 1 [†]	-0.5 (-2.0, 1.0)
	Multivariable-adjusted model 2 [‡]	-0.8 (-2.3, 0.8)
Cataract Diagnosis or Surgery: No (81.1%, n=257)	0 (REF)	0 (REF)
	Univariate analysis	-0.6 (-3.0, 1.7)
Yes (18.9%, n=60)	Multivariable-adjusted model 1 [†]	-0.7 (-2.7, 1.2)
	Multivariable-adjusted model 2 [‡]	-0.6 (-2.6, 1.5)
Macular Degeneration: No (95.6%, n=303)	0 (REF)	0 (REF)
	Univariate analysis	1.3 (-3.3, 5.9)
Yes (4.4%, n=14)	Multivariable-adjusted model 1 [†]	0.3 (-3.3, 4.0)
	Multivariable-adjusted model 2 [‡]	0.5 (-3.3, 4.3)
Cup-to-disc ratio: < 0.6: (42.5%, n=134)	0 (REF)	0 (REF)
0.6 (57.5%, n=183)	-2.5 (-4.3, -0.6)	1.7 (-0.2, 3.6)

	Physical Component Summary	Mental Component Summary
	Multivariable-adjusted model 1 [†]	0.9 (−0.6, 2.5)
	Multivariable-adjusted model 2 [‡]	0.5 (−1.1, 2.1)
Highest untreated IOP: 22 mm Hg (69.1%, n=219)	0 (REF)	0 (REF)
	Univariate analysis	1.4 (−0.6, 3.5)
< 22 mm Hg (30.9%, n=98)	Multivariable-adjusted model 1 [†]	0.6 (−1.1, 2.3)
	Multivariable-adjusted model 2 [‡]	1.3 (−0.4, 3.1)
VF loss: Peripheral only (57.7%, n=183)	0 (REF)	0 (REF)
	Univariate analysis	2.3 (−0.9, 5.6)
Paracentral only (9.5%, n=30)	Multivariable-adjusted model 1 [†]	2.2 (−0.4, 4.8)
	Multivariable-adjusted model 2 [‡]	1.3 (−1.4, 4.0)
	Univariate analysis	1.3 (−0.7, 3.3)
Paracentral and Peripheral (32.8%, n=104)	Multivariable-adjusted model 1 [†]	1.0 (−0.7, 2.7)
	Multivariable-adjusted model 2 [‡]	1.0 (−0.8, 2.7)
Eyes affected: 1 eye (63.1%, n=200)	0 (REF)	0 (REF)
	Univariate analysis	0.2 (−1.7, 2.2)
2 eyes (36.9%, n=117)	Multivariable-adjusted model 1 [†]	0.1 (−1.5, 1.7)
	Multivariable-adjusted model 2 [‡]	0.4 (−1.2, 2.1)
Treatment pattern: Drops or pills only (65.3%, n=207)	0 (REF)	0 (REF)
Laser Trabeculoplasty [§] (16.1%, n= 51)	−1.1 (−3.7, 1.4)	−2.6 (−5.2, −0.1)

	Physical Component Summary	Mental Component Summary
Trabeculectomy [/] (6.3%, n= 20)	Multivariable-adjusted model 1 [†]	-3.0 (-5.1, -0.9)
	Multivariable-adjusted model 2 [‡]	-2.5 (-4.6, -0.3)
	Univariate analysis	3.1 (-0.7, 7.0)
	Multivariable-adjusted model 1 [†]	0.6 (-2.5, 3.7)
	Multivariable-adjusted model 2 [‡]	0.8 (-2.4, 4.1)

Abbreviations: POAG = Primary Open-Angle Glaucoma; SD = Standard Deviation; IOP = Intraocular Pressure; VF: visual field, REF: reference group

* A positive value in the difference in change score means that a characteristic is associated with a *slower* decline over 4 years and a negative value in the difference in change scores means that a characteristic is associated with a *faster or worse* decline.

[†] Multivariable –adjusted model 1 – All listed variables above were simultaneously adjusted for in all models and additionally adjusted for specific health-related quality of life score as of first assessment (pre-diagnosis), age as of return of pre-diagnosis biennial questionnaire (years), date of diagnosis, period (1992–1996, 1996–2000), time between pre- and post-diagnosis biennial questionnaire return dates (months), time between pre-diagnosis questionnaire return to diagnosis date (months)

[‡] Multivariable-adjusted model 2 – In addition to covariates adjusted for in Model 1, also adjusted for highest attained education level (RN, Bachelors, Master's or above), husband's highest attained education level (high school, college, graduate degree), marital status (married, non-married), living status (living alone or with other(s)), body mass index (<22, 22–23, 24–25, 26–27, 28–29, 30+ kg/m²), cigarette smoking (never smoking, 1–9, 10–19, 20–29, 30+ pack-years), physical activity (quartiles of metabolic equivalent-hours per week), age at menopause (<45, 45–50, 51–53, 54+ years), postmenopausal hormone use (never user, past, current user), self-reported physician diagnosed hypertension, diabetes, hypercholesterolemia, myocardial infarction, osteoarthritis or rheumatoid arthritis, depression, chronic respiratory conditions (emphysema, asthma or chronic bronchitis).

[§] Laser trabeculectomy refers to any report of laser trabeculectomy with or without drops or pills but without any trabeculectomy. Those with missing treatment pattern were included in the analyses but not shown.

[/] Trabeculectomy refers to any report of trabeculectomy with or without drops or pills or laser trabeculectomy. Those with missing treatment pattern were included in the analyses but not shown.

Table 3

Stratum specific differences in change (95% confidence interval) over 4 years from multivariable linear regression models* for selected characteristics in relation to physical and mental component summary scores and interactions with family history and number of eyes affected (n=317)

Stratum	N	Comparison	Physical Component Summary	p for interaction	Mental Component Summary	p for interaction
Family History –	173	2 eyes affected vs. 1 eye affected	1.1 (–1.9, 4.0)		2.4 (–0.1, 4.9)	
Family History +	144	2 eyes affected vs. 1 eye affected	–0.1 (–3.6, 3.3)	0.76	–1.8 (–4.4, 0.7)	0.02
Family History –	173	Laser trabeculoplasty [†] vs. drops or pills	–1.4 (–5.5, 2.6)		–0.2 (–3.6, 3.2)	
Family History +	144	Laser trabeculoplasty [†] vs. drops or pills	1.1 (–2.9, 5.1)	0.33	–5.2 (–8.2, –2.1)	0.04
Family History –	173	Trabeculectomy [‡] vs. drops or pills	–2.4 (–8.3, 3.6)		4.4 (–0.5, 9.4)	
Family History +	144	Trabeculectomy [‡] vs. drops or pills	0.4 (–6.2, 7.0)	0.49	–2.3 (–7.3, 2.7)	0.44
1 eye affected	200	Laser trabeculoplasty [†] vs. drops or pills	0.8 (–3.0, 4.5)		0.5 (–2.0, 3.0)	
2 eyes affected	117	Laser trabeculoplasty [†] vs. drops or pills	0.7 (–4.0, 5.4)	0.88	–5.5 (–9.7, –1.2)	0.001
1 eye affected	200	Trabeculectomy [‡] vs. drops or pills	–0.1 (–5.7, 5.5)		2.7 (–1.0, 6.4)	
2 eyes affected	117	Trabeculectomy [‡] vs. drops or pills	1.7 (–5.1, 8.5)	0.89	–2.4 (–8.5, 3.7)	0.64

* Adjusted for the same covariates as specified for Model 2 in Table 2 footnotes

[†] Laser trabeculoplasty refers to any report of laser trabeculoplasty with or without drops or pills but without any trabeculectomy. Those with missing treatment pattern were included in the analyses but not shown.

[‡] Trabeculectomy refers to any report of trabeculectomy with or without drops or pills or laser trabeculectomy. Those with missing treatment pattern were included in the analyses but not shown.

Table 4

Difference in change (95% confidence interval) over 4 years in 8 SF-36 domain scores by pre-diagnosis characteristics, ophthalmological characteristics at diagnosis and treatment history in participants with incident POAG from 1992 – 2000 (n=317)

		Physical Functioning	Role limitations due to Physical Functioning	Bodily pain	General Health	Mental health	Role limitations due to Emotional Issues	Social Functioning	Vitality
Before diagnosis (mean, SD)		48.9 (8.6)	46.8 (11.6)	48.0 (9.6)	52.7 (9.8)	52.1 (7.9)	50.5 (9.3)	52.5 (8.7)	50.9 (9.3)
After diagnosis (mean, SD)		46.4 (10.1)	45.4 (12.2)	47.1 (9.6)	51.8 (9.3)	53.0 (7.0)	50.7 (8.7)	53.0 (8.1)	50.2 (9.1)
Family History: No (54.6%, n=173)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
Yes (45.4%, n=144)	Model 1 *	0.1 (-1.6, 1.9)	-0.5 (-2.8, 1.8)	-0.5 (-2.2, 1.3)	0.3 (-1.2, 1.9)	-0.8 (-2.2, 0.6)	-0.8 (-2.6, 1.0)	-0.9 (-2.6, 0.7)	1.0 (-0.7, 2.7)
	Model 2 †	0.6 (-1.3, 2.4)	-0.9 (-3.4, 1.5)	-0.3 (-2.1, 1.6)	0.2 (-1.5, 1.9)	-0.7 (-2.2, 0.7)	-1.2 (-3.0, 0.7)	-1.1 (-2.8, 0.7)	1.3 (-0.5, 3.1)
Cataract Diagnosis or Surgery: No (81.1%, n=257)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
Yes (18.9%, n=60)	Model 1	-0.9 (-3.3, 1.4)	-1.1 (-4.2, 2.0)	-2.4 (-4.8, -0.1)	-0.2 (-2.3, 1.9)	-0.9 (-2.7, 1.0)	-0.1 (-2.4, 2.3)	-3.3 (-5.5, -1.0)	-0.1 (-2.4, 2.2)
	Model 2	-1.1 (-3.5, 1.3)	-0.8 (-4.0, 2.3)	-2.0 (-4.4, 0.4)	-0.5 (-2.7, 1.6)	-0.6 (-2.5, 1.3)	0.2 (-2.1, 2.6)	-3.1 (-5.3, -0.8)	-0.4 (-2.7, 1.9)
Macular Degeneration: No (95.6 %, n=303)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
Yes (4.4%, n=14)	Model 1	1.0 (-3.3, 5.2)	-3.1 (-8.7, 2.5)	1.4 (-2.8, 5.7)	-1.9 (-5.7, 1.8)	1.1 (-2.2, 4.4)	-1.8 (-6.1, 2.5)	2.9 (-1.2, 7.0)	-1.5 (-5.6, 2.6)
	Model 2	1.9 (-2.6, 6.5)	-3.7 (-9.7, 2.3)	1.9 (-2.6, 6.5)	-2.1 (-6.2, 2.0)	0.7 (-2.8, 4.2)	-1.4 (-5.9, 3.0)	3.5 (-0.7, 7.8)	-1.0 (-5.3, 3.3)
Cup-to-disk ratio: < 0.6 (42.5%, n=134)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
0.6 (57.5%, n=183)	Model 1	-0.8 (-2.7, 1.0)	-1.3 (-3.8, 1.1)	-0.9 (-2.7, 0.9)	-0.6 (-2.2, 1.0)	0.7 (-0.7, 2.1)	0.5 (-1.3, 2.4)	0.6 (-1.1, 2.4)	0.2 (-1.5, 2.0)
	Model 2	-1.3 (-3.2, 0.6)	-1.3 (-3.8, 1.2)	-1.0 (-2.9, 0.9)	-1.3 (-3.0, 0.4)	0.3 (-1.1, 1.8)	-0.1 (-2.0, 1.8)	0.4 (-1.3, 2.2)	-0.5 (-2.3, 1.3)
Highest IOP: 22 mm Hg (69.1%, n=219)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
< 22 mm Hg (30.9%, n=98)	Model 1	1.0 (-1.0, 3.0)	-0.5 (-3.2, 2.1)	-0.7 (-2.7, 1.3)	-0.1 (-1.8, 1.7)	-0.3 (-1.9, 1.2)	1.4 (-0.6, 3.4)	0.4 (-1.5, 2.3)	0.9 (-1.0, 2.8)
	Model 2	1.3 (-0.8, 3.4)	-0.1 (-2.9, 2.7)	-0.2 (-2.3, 1.9)	0.3 (-1.6, 2.1)	0.0 (-1.7, 1.6)	2.2 (0.2, 4.3)	1.2 (-0.8, 3.1)	1.5 (-0.5, 3.5)
VF loss: Periphereal only (57.7%, n=183)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)

		Physical Functioning	Role limitations due to Physical Functioning	Bodily pain	General Health	Mental health	Role limitations due to Emotional Issues	Social Functioning	Vitality
Paracentral only (9.5%, n=30)	Model 1	0.0 (-3.0, 3.1)	1.8 (-2.3, 5.9)	-0.4 (-3.5, 2.6)	1.0 (-1.7, 3.7)	2.5 (0.1, 4.9)	2.4 (-0.7, 5.6)	-0.9 (-3.8, 2.1)	1.4 (-1.5, 4.4)
	Model 2	0.8 (-2.5, 4.1)	2.3 (-2.0, 6.6)	0.7 (-2.6, 3.9)	0.5 (-2.5, 3.4)	1.8 (-0.8, 4.3)	1.8 (-1.4, 5.0)	-0.8 (-3.9, 2.3)	1.5 (-1.6, 4.6)
Paracentral and Peripheral (32.8%, n=104)	Model 1	0.1 (-1.9, 2.2)	-0.3 (-3.0, 2.3)	-1.2 (-3.2, 0.8)	-0.6 (-2.3, 1.2)	0.9 (-0.6, 2.5)	0.7 (-1.3, 2.8)	0.6 (-1.3, 2.5)	-0.1 (-2.1, 1.8)
	Model 2	0.0 (-2.1, 2.1)	-0.9 (-3.6, 1.9)	-1.5 (-3.6, 0.6)	-0.6 (-2.5, 1.3)	0.3 (-1.4, 2.0)	1.0 (-1.1, 3.1)	0.8 (-1.2, 2.8)	-0.4 (-2.4, 1.7)
Eyes affected: 1 eye (63.1%, n=200)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
2 eyes (36.9%, n=117)	Model 1	1.7 (-0.2, 3.6)	-0.1 (-2.5, 2.4)	0.5 (-1.4, 2.3)	0.5 (-1.2, 2.2)	-0.1 (-1.6, 1.4)	0.4 (-1.5, 2.4)	-0.1 (-1.9, 1.7)	1.0 (-0.8, 2.8)
	Model 2	1.9 (-0.1, 3.9)	0.5 (-2.1, 3.2)	1.2 (-0.8, 3.2)	0.5 (-1.3, 2.3)	0.3 (-1.3, 1.8)	0.5 (-1.5, 2.4)	0.5 (-1.4, 2.3)	2.1 (0.2, 3.9)
Treatment: Drops and pills (65.3%, n=207)		0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)	0 (REF)
Laser Trabeculectomy [‡] (16.1%, n= 51)	Model 1	-0.5 (-3.0, 1.9)	-1.7 (-5.0, 1.5)	-1.7 (-4.2, 0.8)	-0.4 (-2.6, 1.7)	-2.6 (-4.5, -0.7)	-2.6 (-5.1, -0.1)	-2.7 (-5.1, -0.4)	-1.3 (-3.7, 1.1)
	Model 2	0.0 (-2.5, 2.6)	-0.8 (-4.1, 2.5)	-1.2 (-3.7, 1.3)	-0.4 (-2.7, 1.8)	-2.4 (-4.4, -0.4)	-1.8 (-4.2, 0.7)	-1.6 (-4.0, 0.7)	-1.0 (-3.4, 1.5)
Trabeculectomy [§] (6.3%, n= 20)	Model 1	1.6 (-2.0, 5.2)	1.4 (-3.3, 6.2)	0.7 (-2.9, 4.3)	1.5 (-1.7, 4.7)	0.1 (-2.7, 2.9)	1.5 (-2.1, 5.2)	1.7 (-1.8, 5.2)	1.4 (-2.1, 4.9)
	Model 2	2.0 (-1.9, 5.8)	-0.2 (-5.2, 4.8)	-0.8 (-4.6, 3.0)	1.6 (-1.9, 5.0)	0.1 (-2.8, 3.1)	1.4 (-2.3, 5.2)	1.0 (-2.6, 4.6)	1.6 (-2.1, 5.2)

Abbreviations: POAG = Primary Open-Angle Glaucoma; SD = Standard Deviation; IOP = Intraocular Pressure; VF= visual field, REF: reference group

^{*} Multivariable adjusted model 1 – All listed variables above were simultaneously adjusted for in all models and additionally adjusted for specific health-related quality of life score as of first assessment (pre-diagnosis), age as of return of pre-diagnosis biennial questionnaire (years), date of diagnosis, period (1992–1996, 1996–2000), time between pre- and post-diagnosis biennial questionnaire return dates (months), time between pre-diagnosis questionnaire return to diagnosis date (months)

[†] Multivariable adjusted model 2 – In addition to covariates adjusted for in Model 1, also adjusted for highest attained education level (RN, Bachelors, Master's or above), husband's highest attained education level (high school, college, graduate degree), marital status (married, non-married), living status (living alone or with other(s)), body mass index (<22, 22–23, 24–25, 26–27, 28–29, 30+ kg/m²), cigarette smoking (never smoking, 1–9, 10–19, 20–29, 30+ pack-years), physical activity (quartiles of metabolic equivalent-hours per week), age at menopause (<45, 45–50, 51–53, 54+ years), postmenopausal hormone use (never user, past, current user), self-reported physician diagnosed hypertension, diabetes, hypercholesterolemia, myocardial infarction, osteoarthritis or rheumatoid arthritis, depression, chronic respiratory conditions (emphysema, asthma or chronic bronchitis).

[‡] Laser trabeculectomy refers to any report of laser trabeculectomy with or without drops or pills but without any trabeculectomy. Those with missing treatment pattern were included in the analyses but not shown.

[§] Trabeculectomy refers to any report of trabeculectomy with or without drops or pills or laser trabeculectomy. Those with missing treatment pattern were included in the analyses but not shown.