Improving health-related quality of life in glaucoma during 11 years and its association with vision loss and treatment of the disease

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ABSTRACT.

Purpose: To evaluate the impact of glaucoma on health-related quality of life (HRQoL) and mental health in the ageing population of Finland.

Methods: Altogether 7380 and 5774 Finnish individuals aged 30 years and older with known eye disease status were studied in 2000 and 2011, respectively, in two population-based surveys, including an 11-year follow-up of 4683 participants. Data on HRQoL (EQ-5D-3L, 15D), depression (BDI), psychological distress (GHQ-12) and eye disease diagnoses were obtained from self-reported assessments. Information on glaucoma was complemented with the medication, diagnosis and eye surgery data obtained from the Finnish Health Registries. Distance visual acuity was assessed using the Snellen eye chart test. In logistic regression analyses, data were corrected for age, gender and the most common comorbidities.

Results: Glaucoma patients with verified diagnosis ($n = 192$ in 2000, $n = 202$ in 2011) and individuals with self-suspected glaucoma ($n = 100$ in 2000, $n = 41$ in 2011) showed a significant decrease in their HRQoL. Glaucoma was also associated with worsened overall mental health based on BDI and GHQ-12 results. Visual impairment associated with glaucoma is the major determinant of the reduced HRQoL and mental health. Neither glaucoma medication nor glaucoma surgery affected these parameters. The impact of glaucoma on HRQoL and mental health diminished between 2000 and 2011 in a cross-sectional setting. The newly diagnosed glaucoma during the 11-year follow-up had a minimal effect on them.

Conclusion: Glaucoma patients show reduced HRQoL and mental health, which is associated with vision loss regardless of the awareness or treatment of the disease. However, this effect seems to be diminishing over time, and the newly diagnosed glaucoma did not show a significant effect on either HRQoL or mental health.

Key words: epidemiology – glaucoma – health-related quality of life – impaired vision – mental health – population survey

Introduction

Glaucoma is a chronic disease characterized by the progressive degeneration of retinal ganglion cells (Weinreb et al. 2014). It is the second leading cause of irreversible loss of vision worldwide, affecting more than 60 million individuals in the world, with approximately 16% being bilaterally blind (Forsman et al. 2007; Peters et al. 2013). However, the number may be higher as the disease can remain asymptomatic until a relatively late stage (Weinreb et al. 2014). The pathogenesis of glaucoma is not fully understood. However, the level of intraocular pressure is related to retinal ganglion cell degeneration (Weinreb et al. 2014). At the moment, the only proven method to treat the disease is the reduction of intraocular pressure, usually via ocular hypotensive drugs, laser treatment and surgery (Weinreb et al. 2014). In addition to elevated intraocular pressure, other risk factors for glaucoma include old age, myopia, exfoliation and African ethnicity (Quigley & Broman 2006; Weinreb et al. 2014).

The impact of glaucoma on the quality of life (QoL), mental health and visual acuity (VA) has been previously assessed in many countries through cross-sectional studies. However, most of these studies have utilized vision-related QoL instruments, and therefore, the results may not be generalizable (Freeman et al. 2008;

Medeiros et al. 2015; Jones et al. 2017; Machado et al. 2019). Furthermore, studies that have utilized more generic health-related quality of life (HRQoL) instruments that evaluate physical, psychological and functional well-being, lack longitudinal setting or have a small study population (Wolfram et al. 2013; Jung & Park 2016).

To answer these unmet needs, our aim in this study was to evaluate the impact of glaucoma on generic HRQoL and mental health, and the cross-sectional and longitudinal differences in these parameters in the Finnish adult population during an 11-year follow-up. We utilized two commonly used generic HRQoL-based instruments, EuroQol-5 Dimension (EQ-5D-3L) (Brooks 1996; Dolan 1997) and 15D (Sintonen 1995; Sintonen 2001). Because these instruments have a limited spectrum on mental health, we included Beck Depression Inventory (BDI) (Beck & Beck 1972) and General Health Questionnaire-12 (GHQ-12) (Goldberg 1972; Pevalin 2000) that evaluate depression and psychological distress.

Materials and methods

Study design

We used two nationwide health examination surveys carried out by the Finnish Institute for Health and Welfare. They represent the Finnish adult population at two different time points: the first one was carried out in 2000–2001 and a follow-up in 2011. Both the surveys included home interviews and comprehensive health examinations conducted at a nearby screening centre. If the invited participants did not attend the health examination, an abridged examination was conducted at home or in an institution. The Health 2000 Survey analysed a sample of 9922 adults aged 18 years or over living in mainland Finland. The sample was selected by a stratified two-stage cluster sampling design. The Health 2011 Survey included all living participants of the Health 2000 Survey, who agreed to be contacted and were aged 29 years or over. In addition, a new sample of 1994 young adults aged 18–28 years was also included. More detailed information has been published previously (Aromaa & Koskinen 2004; Koskinen et al. 2012). For the

current study, we have only included participants aged 30 years and older. Both the surveys provided a probability-clustered sampling and weighting scheme, which estimates the health statistics that are representative of Finnish adult population aged 30 years and older at the time of sampling (Heistaro 2008; Lundqvist & Mäki-Opas 2016). The sampling scheme also accounts for designed oversampling of people aged 80 years and older in the 2000 survey baseline to correct the low participation rate of elder adults. The unweighted participation rate was 93% in the Health 2000 Survey while in the follow-up it was 73%. Different weights were applied to both the surveys to account for the loss between the two time points (Härkänen et al. 2016).

Both the survey samples were linked to the Social Insurance Institution of Finland (Kela) registers to obtain data on the reimbursement for glaucoma medication (data available from 1965 to 2011) and the number of glaucoma medication prescriptions (data available from 1999 to 2011). We also included data of different glaucoma diagnoses and eye operations obtained from the Care Registers for Social Welfare and Health Care (HILMO). This data included inpatient care (HILMO data, available from 1968 to 2011) and outpatient visits (AvoHILMO data, available from 1997 to 2011).

Assessment of glaucoma status

Both the surveys included an interview with the following questions on eye diseases: 'Has a doctor diagnosed you with one of the following diseases: cataract, glaucoma, retinal degeneration or other visual defect or injury'? The participants who had answered to eye disease questionnaire and/or had register data on glaucoma were included in the 'eye disease status known' group.

Individuals suffering from glaucoma were evaluated using three categories. The first category, 'self-reported glaucoma', included participants who reported having glaucoma in the survey questionnaire. The second category, 'verified glaucoma', included participants that fall into one of these following conditions: (1) were granted special reimbursement for glaucoma medication by Kela; (2) with a high number (>10) of glaucoma medication prescriptions

between 1999–2000 (2000 survey) or 1999–2011 (2011 survey); (3) had glaucoma medication prescriptions since 2011 (2011 survey); (4) had a verified glaucoma diagnosis according to the HILMO/AvoHILMO data (International Classification of Diseases diagnosis codes 37500–37520, 37598–37599 for version 8, 3651–3659 for version 9, and H40, H40.1–H40.9 for version 10); or (5) had undergone at least one of the following eye operations according to the HILMO/AvoHILMO data: trabeculectomy and iridectomy, glaucoma shunt operation, non-penetrating glaucoma surgery, other filtering operation and transscleral laser coagulation of ciliary body. These conditions were used as some individuals had glaucoma medication prescriptions only for a short duration, indicating they were suffering from another disease than chronic glaucoma. The third category, 'self-suspected glaucoma', consisted of participants who had self-reported glaucoma but did not belong to the verified glaucoma category. This classification is shown in Table 1. 'Glaucoma negatives' group included individuals with a known eye disease status but did not belong to any of the above mentioned three glaucoma categories. For the analyses, we also separated 'glaucoma medication' group that included all glaucoma patients with glaucoma medication prescriptions, and 'glaucoma operated' group with verified glaucoma patients that had undergone at least one of the listed eye operations or had self-reported glaucoma operation in the survey questionnaire.

Assessment of health-related quality of life

Health-related quality of life (HRQoL) was evaluated using two generic preference-based instruments, a three-level version of EuroQol-5 Dimension (EQ-5D-3L, later referred to as EQ-5D) and 15D. EQ-5D is a self-administered questionnaire comprising of one question for each of the five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each question contains three answers on a scale of 1 (no difficulties) to 3 (extreme difficulties). These scores can then be converted into EQ-5D index scores on a scale between 0 (representing HRQoL equal to being dead) and 1 (representing the best possible HRQoL). We used EQ-5D weighted with UK time trade-off

Table 1. Classification of glaucoma in Health 2000 and 2011 surveys.

	Classification conditions for 2000 survey	Classification conditions for 2011 survey
Glaucoma, self-reported	Reported glaucoma in the questionnaire	Reported glaucoma in the questionnaire
Glaucoma, verified	Granted special reimbursement for glaucoma medication by Kela in 2000 or before OR High number (>10) of glaucoma medication prescriptions between 1999 and 2000 (Kela) OR Verified glaucoma diagnosis between 1968 and 2000 (HILMO/AvoHILMO) OR Undergone eye operation due to glaucoma between 1997 and 2000 (HILMO/AvoHILMO)	Granted special reimbursement for glaucoma medication by Kela in 2011 or before OR High number (>10) of glaucoma medication prescriptions between 1999 and 2011 (Kela) OR Verified glaucoma diagnosis between 1968 and 2011 (HILMO/AvoHILMO) OR Undergone eye operation due to glaucoma between 1997 and 2011 (HILMO/AvoHILMO) OR Glaucoma medication prescriptions since 2011
Glaucoma, self-suspected	Self-reported glaucoma, but not included in the verified glaucoma group	Self-reported glaucoma, but not included in the verified glaucoma group

HILMO/AvoHILMO, Care Registers for Social Welfare and Health Care; Kela, Social Insurance Institution of Finland.

weights on a scale between −0.59 (representing HRQoL equal to being dead) and 1 (representing the best possible HRQoL) to improve comparability with other populations (Dolan 1997). A difference of ≥0.07 is considered to be clinically meaningful (Walters & Brazier 2005). 15D is a Finnish preference-based measure of HRQoL consisting of 15 dimensions/questions – mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity. Each question contains five answer options on a scale of 1 (no difficulties) to 5 (extreme difficulties). A single index score is obtained by weighting the scores with population-based preference weights (Sintonen 2001). We used Finnish preference weights with a scale between 0 (representing HRQoL equal to being dead) and 1 (representing the best possible HRQoL). A difference of ≥0.015 is considered to be clinically meaningful (Alanne et al. 2015).

Assessment of mental health

Both the surveys included two self-reported instruments that evaluate mental health, Beck Depression Inventory (BDI) and General Health Questionnaire-12 (GHQ-12). Beck Depression Inventory (BDI) is used to assess depression (Beck & Beck 1972) and GHQ-12 evaluates 12 dimensions of psychological distress, including depression, anxiety, social interaction and confidence (Goldberg 1972; Pevalin 2000). In the 2000 survey, a 21-item BDI-21 was used, whereas in the 2011 survey a shorter version, a 13-item BDI-13 was used (Aalto et al. 2012). The answers for GHQ-12 were dichotomized according to whether difficulties were presented or not (0 = no, 1 = yes). A total score was calculated for all the three instruments on a scale of 0 to 63 for BDI-21, 0 to 39 for BDI-13 and 0 to 12 for GHQ-12. Higher score points indicate major depression or psychological distress. Total scores of ≥10 for BDI-21, ≥5 for BDI-13 and >3 for GHQ-12 are used as cut-off points indicative of depression or psychological distress (Beck et al. 1988; Aromaa & Koskinen 2004; Koskinen et al. 2012).

Visual acuity tests

Both the surveys included a habitual distance VA measurement by a study nurse binocularly at 4 m, with current vision correction. Illumination was set to ≥350 lux on the modified logMAR letter chart published by Precision Vision (Ferris et al. 1982; Heistaro 2008; Lundqvist & Mäki-Opas 2016). All VA values were presented as decimal (Snellen) equivalents. Low VA values that could not have been determined were reported as 0.01. We used the following classifications: VA ≥ 1.0 (good vision), VA 0.63–0.8 (adequate vision), VA 0.32–0.5 (weak vision), VA 0.125–0.25 (impaired vision), and VA < 0.1 (severe vision loss or blindness) (World Health Organization 2018). Habitual distance VA ≤ 0.25 was considered as impaired vision.

Comorbidities

To eradicate the potential effect of common diseases on HRQoL, self-reported diseases in both the surveys were categorized into major comorbidity groups according to Taipale and co-workers (Taipale et al. 2019) and our previous study (Purola et al. 2021). These include heart diseases (myocardial infarction, angina pectoris, heart failure, arrhythmias and 'other heart disorders'), respiratory diseases (asthma, chronic obstructive pulmonary disease, chronic bronchitis and 'other pulmonary disease'), vascular diseases (stroke and varicose veins in lower limbs), musculoskeletal conditions (rheumatoid arthritis, osteoarthrosis, fractures and osteoporosis), and psychiatric conditions (psychotic disorders, depression, anxiety, psychoactive substance abuse and 'other psychiatric disease'). Moreover, hypertension, diabetes, Parkinson's disease and unspecified cancer were each categorized as a separate group. An individual was considered to have comorbidity if they reported having any of the conditions included in the comorbidity groups.

Statistical analyses

All analyses were performed using R software version 3.5.1 (R Core Team, R Foundation for Statistical Computing, Austria). Our data included both the survey samples, which were used for cross-sectional and longitudinal analyses. We used Survey package 3.37 for R (Lumley 2004) and weighting scheme calculated by the Finnish

Institute for Health and Welfare to account for the sampling design, the oversampling of individuals aged 80 years and older, and the loss to follow-up. For the prevalence and incidence analyses, we estimated population totals and ratios using functions *svytotal* and *svyratio* included in the Survey package. Individuals with missing data in analysed variables were excluded. Because the data of the continuous variables were non-normally distributed, we used Mann–Whitney U test for between-group comparisons, Wilcoxon's signed-rank test to compare the matched pairs, and the Kruskal–Wallis test to compare multiple groups. Odds ratios (ORs) with 95% confidence intervals were calculated using logistic regression analysis, corrected for age, gender and comorbidities. For all analyses, a two-tailed p-value of <0.05 was considered as the cut-off for statistical significance.

Informed consent

All procedures in the Health 2000 and 2011 studies involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee, and the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethical approval process details are discussed in previous publications (Heistaro 2008; Lundqvist & Mäki-Opas 2016). All the participants received an information letter regarding the study beforehand. Two informed consents were obtained at the beginning of the study from everyone: one for the health interview and the other for the health examinations (Heistaro 2008). The participants were provided with appropriate information concerning the study and asked to sign an informed consent again before the follow-up examination in 2011 (Lundqvist & Mäki-Opas 2016).

Results

Study population

In total, 8028 individuals aged 30 years and older participated in the 2000 survey, 8006 in the 2011 survey, and 6360 in both the surveys. Of these individuals, 7380 and 5774 had known eye disease status in 2000 and 2011,

respectively, and 4683 individuals took part in both the time points and were included in the 11-year follow-up study. The number of self-reported glaucoma patients was 258 in 2000 and 160 in 2011, verified glaucoma patients 192 in 2000 and 202 in 2011, and self-suspected glaucoma patients 100 in 2000 and 41 in 2011 (Fig. S1). The flow chart of the glaucoma patient selection in both the time points is shown in Fig. 1. The number, mean age and gender distribution of the study population are shown in Table 2, as well as the available data on HRQoL, mental health and distance VA of the individuals with known eye disease status.

Prevalence and incidence of glaucoma

The estimated total prevalence and incidence of the three glaucoma groups in the Finnish adult population in 2000 and 2011 are shown in Table 3, and by age and gender in Fig. 2. The prevalence and incidence of glaucoma increased with age in verified and self-reported glaucoma patients in both the time points, but the association with

age was less evident in self-suspected glaucoma patients. The prevalence and incidence of self-reported glaucoma and self-suspected glaucoma were higher in women in both the time points, but this difference in gender distribution was less prevalent in verified glaucoma patients. The percentage of different glaucoma diagnoses in the Finnish adult population in both the time points was estimated using HILMO data, which is shown in Table S1.

Cross-sectional impact of glaucoma on health-related quality of life and mental health

EQ-5D and 15D mean scores were significantly reduced in the three glaucoma groups compared to glaucoma negatives in both the time points, as shown in Figs 3A and B. Glaucoma treatment groups also showed statistically significant worsening in both the time points. All glaucoma groups showed clinically meaningful worsening in these factors when compared to glaucoma negatives in both the time points.
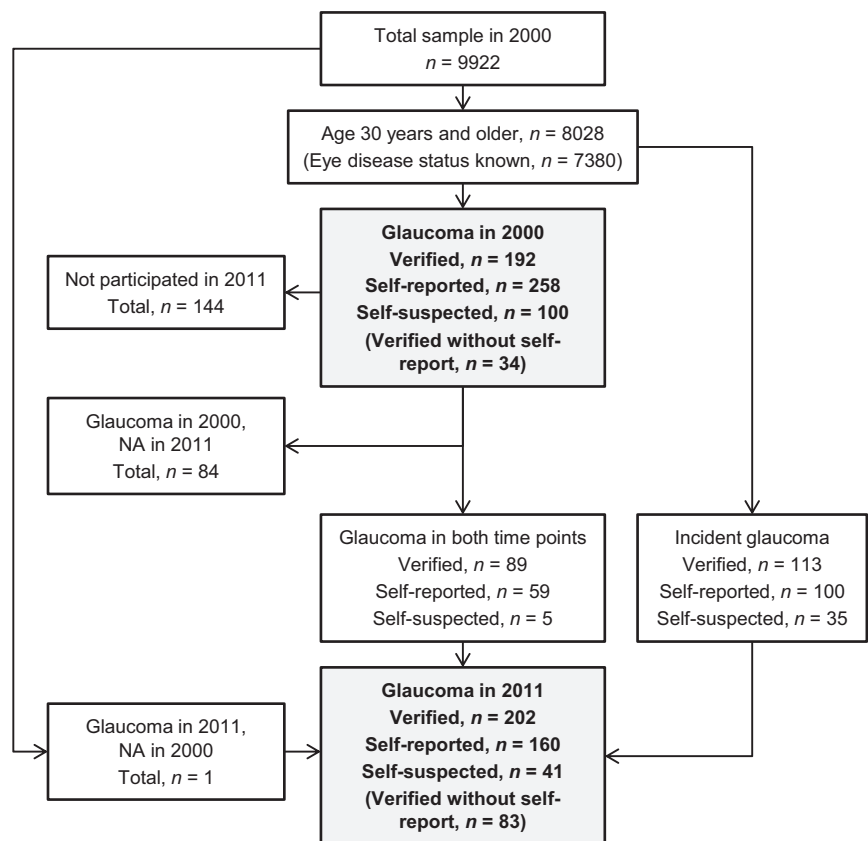

Fig. 1. Selection of the three glaucoma groups in 2000 and 2011. NA = not applicable.

Table 2. Summary of the study population aged 30 years and older.

	2000			2011			11-year follow-up group in 2011[a]		
	n	Mean age (SD)	% women	*n*	Mean age (SD)	% women	*n*	Mean age (SD)	% women
Eligible sample	8028	54.2 (16.2)	54.7	8006	55.3 (15.6)	53.0	6360	60.6 (12.9)	55.5
Eye disease status known	7380	54.2 (16.1)	55.2	5774	55.8 (14.7)	55.7	4683	60.3 (12.2)	56.0
Glaucoma, self-reported	258	71.1 (13.6)	75.2	160	72.0 (11.2)	66.9	159	72.2 (10.8)	66.7
Glaucoma, verified	192	74.4 (11.4)	71.4	202	75.1 (10.7)	67.8	201	75.1 (10.7)	67.7
Glaucoma, self-suspected	100	67.2 (15.5)	81.0	41	65.2 (13.9)	80.5	40	66.0 (13.1)	80.0
Glaucoma, medication	143	73.7 (13.4)	72.7	186	75.5 (11.9)	67.2	185	75.5 (11.6)	67.0
Glaucoma, operated	59	74.5 (11.7)	67.8	38	74.8 (11.2)	55.3	38	74.8 (11.2)	55.3
Special reimbursement for glaucoma medication	177	74.6 (11.4)	71.2	175	76.1 (10.2)	67.4	174	76.0 (10.2)	67.2
Glaucoma negatives	7088	53.5 (15.8)	54.4	5531	55.1 (14.3)	55.1	4442	59.5 (11.9)	55.2
Distance VA measured	6644	53.6 (15.5)	55.3	4560	56.5 (14.1)	55.7	3810	60.1 (11.9)	55.5
Impaired distance VA (≤0.25)	147	80.0 (11.7)	74.1	53	76.6 (13.7)	60.4	46	77.6 (13.1)	60.9
EQ-5D index score available	6131	53.5 (15.7)	55.9	4029	55.8 (13.9)	56.3	3086	59.4 (11.7)	56.8
15D index score available	6149	53.2 (15.2)	55.7	4214	56.3 (13.8)	56.2	3462	59.8 (11.6)	56.1
BDI total score available	6297	52.7 (14.9)	55.0	4303	56.1 (13.8)	56.0	3565	59.6 (11.5)	55.7
GHQ-12 total score available	6530	53.2 (15.3)	55.1	4449	56.2 (14.0)	55.8	3689	59.8 (11.7)	55.7

SD = standard deviation, VA = visual acuity.

[a] The follow-up group includes the 2011 eye status of the individuals who had participated in both time points.

Table 3. Estimated prevalence and incidence with 95% confidence intervals (CIs) of the three glaucoma groups in the Finnish population aged 30 years and older in 2000 and 2011

|	2000		2011		Incidence 2000–2011	
	N (95% CI)	Prevalence % (95% CI)	*N* (95% CI)	Prevalence % (95% CI)	*N* (95% CI)	*N*/year/ 10 000 individuals (95% CI)
Glaucoma, verified	75 683 (57 534–93 832)	2.33 (2.19–2.48)	79 758 (60 199–99 317)	2.57 (2.30–2.85)	45 325 (34 490–56 160)	19 (17–20)
Glaucoma, self-reported	100 517 (76 226–124 808)	3.10 (2.95–3.26)	83 453 (64 288–102 618)	2.70 (2.47–2.93)	52 026 (40 359–63 693)	22 (20–23)
Glaucoma, self-suspected	37 349 (27 648–47 050)	1.15 (1.06–1.25)	21 455 (16 245–26 665)	0.69 (0.61–0.77)	18 233 (13 851–22 615)	7 (6–8)

BDI mean scores, visualized in Figs 3C and D were significantly worse in all glaucoma groups compared to glaucoma negatives. For GHQ-12 (Fig. 3E), only the verified glaucoma group in 2000 showed significant worsening (p = 0.037, Mann–Whitney *U* test) compared to glaucoma negatives. All glaucoma groups showed a decrease (p < 0.0001) in the distance VA compared to glaucoma negatives, as shown in Fig. 3F. There was no statistically significant change in the effect of glaucoma on VA when self-reported cataract and retinal degeneration were included as covariates (Table S2).

No significant difference was found between the three glaucoma groups, except in the distance VA in 2000 (p = 0.0002, Kruskal–Wallis test), in which the verified group had the worst value and the self-suspected group the highest. No significant difference was found between treated and untreated glaucoma patients. Impaired distance vision (VA ≤ 0.25) showed a stronger deteriorating impact on both HRQoL and mental health compared to all glaucoma groups. When comparing these parameters between 2000 and 2011, verified and self-reported groups showed an increase (p < 0.01) in EQ-5D, 15D, and distance VA scores, and the verified group showed improvement in GHQ-12 (p = 0.0042). The verified group showed a clinically meaningful increase in both EQ-5D and 15D, and the self-reported group in 15D. Both treatment groups showed

statistically significant improvement in GHQ-12 and distance VA, as well as statistically significant and clinically meaningful improvement in EQ-5D and 15D. Glaucoma negatives had a statistically significant (p < 0.01) but not clinically meaningful increase in these parameters.

Individual EQ-5D and 15D dimensions (difficulties versus no difficulties), as well as BDI and GHQ-12 cut-off points indicative of depression and psychological distress, were assessed using ORs, as shown in Table 4. In 2000, only the self-reported glaucoma group showed an increase in difficulties concerning usual activities according to EQ-5D. In 2011, both verified and self-reported groups showed an increase in difficulties amongst mobility, and the
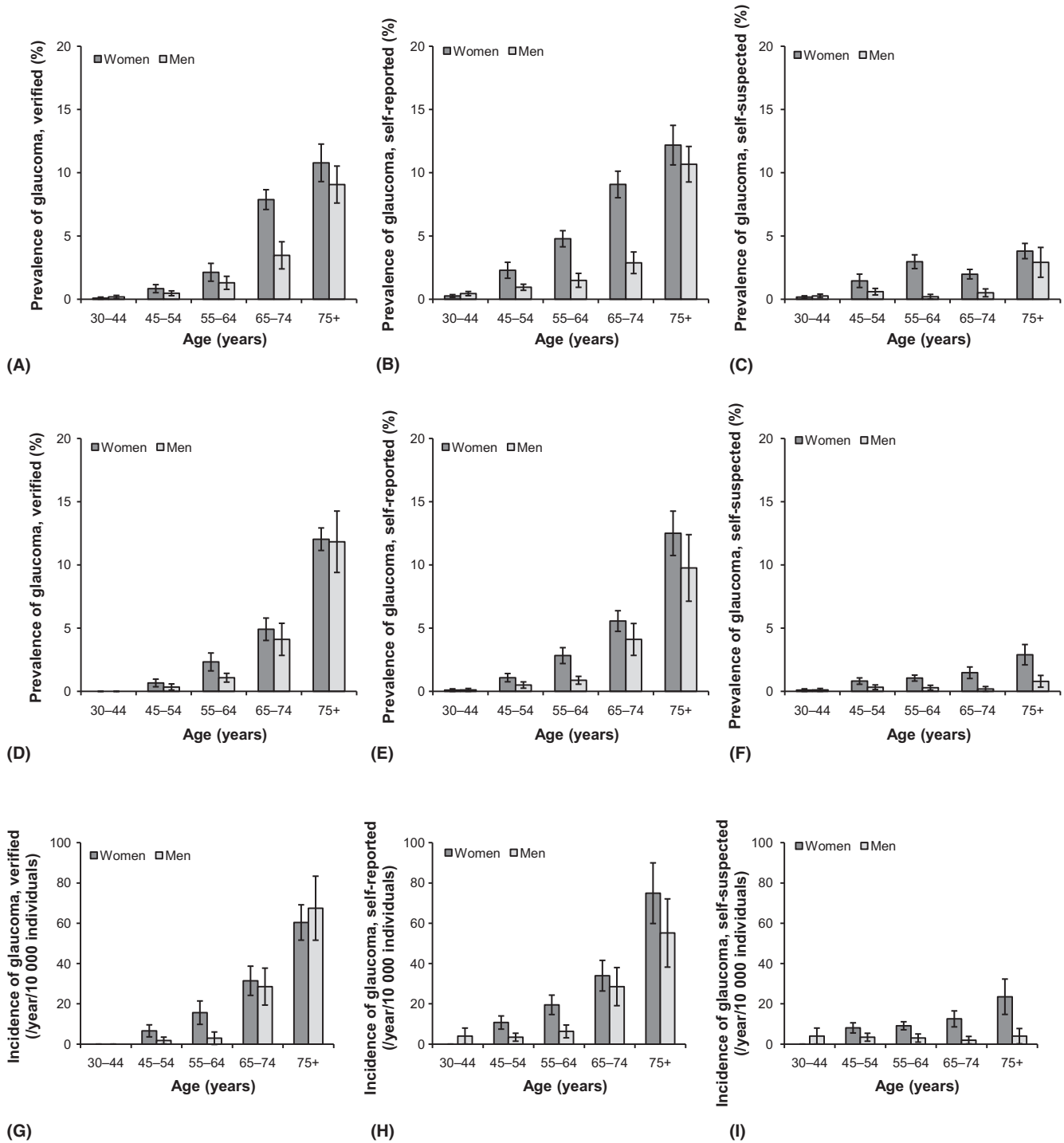
Fig. 2. Estimated prevalence (with 95% confidence intervals) of the three glaucoma groups in the Finnish adult population (age 30 years and older) by age and gender in 2000 (A–C) and 2011 (D–F), and the incidence between 2000 and 2011 (G–I).

self-suspected group in self-care, in the EQ-5D results. When assessing the five most affected 15D dimensions, both verified and self-reported groups showed an increase in difficulties amongst vision and usual activities, and self-suspected group an increase in mobility in 2000 and vision in 2011. In 2011, both verified and self-reported groups showed an increase in

difficulties amongst usual activities and mental function. Verified glaucoma patients who had undergone eye surgery due to the disease showed increased odds for pain and discomfort and difficulties in usual activities compared to untreated glaucoma patients in 2000, but no significant difference was found in 2011 between treated and untreated. When evaluating the odds

for mental health, only the verified glaucoma group showed increased odds for psychological distress in 2000.

The association between glaucoma, HRQoL, mental health and distance VA were observed in both the time points, as shown in Figs S2 and S3. Verified and self-reported glaucoma patients, glaucoma negatives and glaucoma patients with known glaucoma
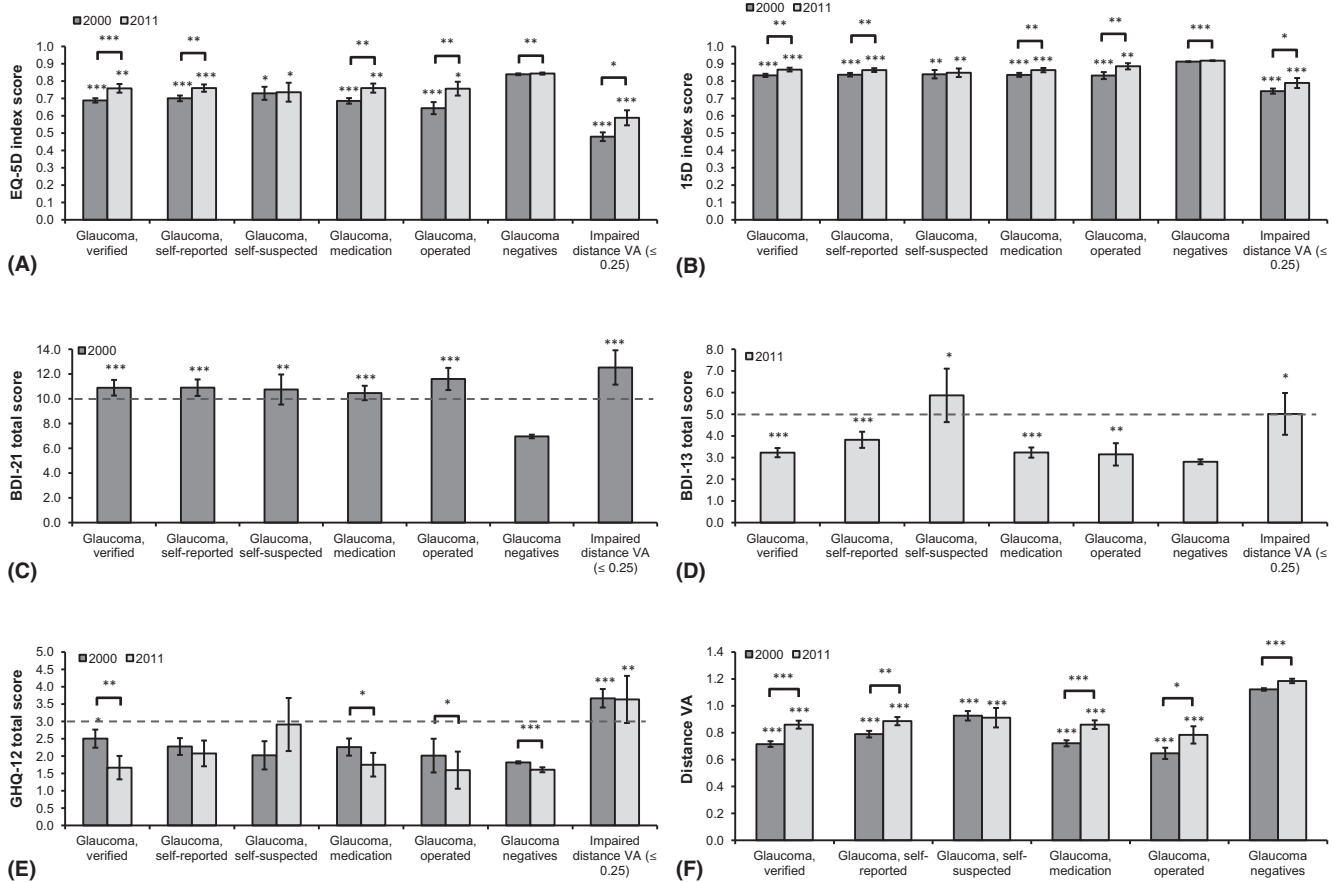
Fig. 3. The index/total score means of EQ-5D (A), 15D (B), BDI (C, D), GHQ-12 (E), and distance visual acuity (VA; F) in glaucoma patients, glaucoma negatives and visually impaired in cross-sectional studies conducted in 2000 and 2011. When calculating statistical significance (Mann–Whitney U test), glaucoma and visual impairment groups were tested against glaucoma negatives within the same year. In addition, mean values were compared between time points in each group. Dashed lines represent clinically meaningful cut-off values for BDI-21 ($\geq$10), BDI-13 ($\geq$5), and GHQ-12 (>3). *Denotes statistical significance with p < 0.05. **Denotes statistical significance with p < 0.01. ***Denotes statistical significance with p < 0.0001.

medication showed a decrease in HRQoL scores and worsening of mental health when their VA diminished. Individual HRQoL dimensions were observed in the 2000 study, as shown in Figs S4 and S5. Usual activities, self-care and mobility showed a similar association with VA in both EQ-5D and 15D, as well as vision in 15D. Self-suspected glaucoma patients and operated glaucoma patients were not included, as the number of individuals with impaired VA was low.

Longitudinal impact of glaucoma on health-related quality of life and mental health

The longitudinal effect of glaucoma on HRQoL during the 11-year follow-up was investigated amongst individuals who had participated in both the surveys. Because the number of self-suspecting glaucoma patients was low,

they were excluded from the longitudinal analyses. Individuals with the same glaucoma status in both the time points are shown in Fig. 4. When investigating HRQoL, verified and self-reported glaucoma groups showed statistically significant (p = 0.024 and p = 0.036, respectively, Wilcoxon signed-rank test) and clinically meaningful decrease between the time points with 15D. Glaucoma negatives showed a decline (p < 0.0001) in EQ-5D and 15D, although there was no clinically meaningful difference. For GHQ-12, only glaucoma negatives showed a significant improvement (p < 0.0001). For distance VA, verified (p = 0.0006) and self-reported (p = 0.035) glaucoma groups and glaucoma negatives (p < 0.0001) showed significant decline.

Newly diagnosed glaucoma patients who were glaucoma negative in 2000 but had been diagnosed with glaucoma

during the 11-year follow-up are shown in Fig. 5. Only the verified group showed statistically significant decline in EQ-5D (p = 0.002) and 15D (p = 0.006), although only 15D had a clinically meaningful decrease. Distance VA had declined in verified (p = 0.011) and self-reported (p = 0.047) glaucoma patients.

Discussion

Participants with a verified glaucoma diagnosis, as well as participants who only suspected to have glaucoma, showed a significant decrease in their generic HRQoL compared to individuals without glaucoma. The decrease was, however, more notable amongst individuals suffering from visual impairment. A similar association between glaucoma patients with visual symptoms and declined QoL has been reported in previous publications,

Table 4. Corrected odds ratios (ORs) for EQ-5D dimensions, most affected 15D dimensions, and mental health scores indicative of depression or psychological distress compared to individuals without glaucoma or glaucoma treatment in 2000 and 2011.

| 2000	EQ-5D dimensions					Five most affected 15D dimensions					Mental health	
	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression	Vision	Usual activities	Mobility	Vitality	Mental function	BDI-21 sum ≥10	GHQ-12 sum >3
Glaucoma, verified	1.37 (0.97–1.92)	0.94 (0.60–1.47)	1.33 (0.92–1.92)	1.04 (0.82–1.34)	1.21 (0.71–2.07)	**2.26 (1.68–3.06)**	**1.80 (1.18–2.75)**	1.27 (0.85–1.92)	1.07 (0.78–1.47)	0.89 (0.60–1.32)	1.15 (0.83–1.60)	**1.37 (1.06–1.76)**
Glaucoma, self-reported	1.42 (0.90–2.23)	1.02 (0.71–1.46)	**1.60 (1.10–2.33)**	1.09 (0.86–1.36)	1.05 (0.65–1.69)	**1.83 (1.34–2.50)**	**1.64 (1.13–2.37)**	1.62 (1.05–2.52)	1.18 (0.82–1.70)	0.97 (0.67–1.40)	1.27 (0.91–1.76)	1.07 (0.80–1.45)
Glaucoma, self-suspected	1.72 (0.81–3.65)	1.34 (0.60–2.96)	1.82 (0.88–3.74)	1.36 (0.82–2.24)	0.79 (0.34–1.79)	1.34 (0.78–2.28)	1.41 (0.61–3.23)	**2.71 (1.40–5.25)**	1.28 (0.65–2.55)	1.06 (0.56–2.00)	1.23 (0.73–2.09)	0.72 (0.39–1.34)
Glaucoma, medication	0.71 (0.36–1.39)	1.08 (0.49–2.39)	0.71 (0.30–1.69)	0.82 (0.49–1.36)	0.82 (0.38–1.77)	1.18 (0.80–1.74)	1.11 (0.50–2.45)	0.66 (0.28–1.56)	0.76 (0.30–1.94)	0.87 (0.44–1.72)	0.76 (0.38–1.50)	0.63 (0.36–1.12)
Glaucoma, operated	1.28 (0.43–3.79)	1.22 (0.61–2.43)	**3.14 (1.46–6.75)**	**2.91 (1.53–5.53)**	1.34 (0.53–3.42)	1.37 (0.68–2.71)	1.23 (0.37–4.13)	0.83 (0.31–2.19)	0.92 (0.31–2.72)	0.58 (0.23–1.46)	1.50 (0.85–2.66)	0.74 (0.38–1.45)

2011	EQ-5D dimensions					Five most affected 15D dimensions					Mental health	
	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression	Vision	Usual activities	Mobility	Vitality	Mental function	BDI-13 sum ≥5	GHQ-12 sum >3
Glaucoma, verified	**1.73 (1.18–2.54)**	1.00 (0.57–1.75)	1.21 (0.71–2.07)	1.02 (0.64–1.62)	0.66 (0.31–1.42)	1.25 (0.65–2.43)	**1.85 (1.30–2.63)**	1.39 (0.96–2.02)	1.42 (0.97–2.08)	**1.45 (1.05–1.99)**	1.25 (0.79–1.96)	1.21 (0.61–2.41)
Glaucoma, self-reported	**1.50 (1.11–2.03)**	1.30 (0.89–1.89)	1.16 (0.65–2.10)	1.06 (0.68–1.64)	0.83 (0.48–1.47)	1.47 (0.83–2.62)	**1.64 (1.12–2.40)**	1.21 (0.95–1.54)	1.56 (1.05–2.31)	**1.49 (1.07–2.08)**	1.26 (0.75–2.10)	1.23 (0.69–2.17)
Glaucoma, self-suspected	1.14 (0.47–2.78)	**2.86 (1.52–5.39)**	1.66 (0.60–4.64)	1.22 (0.64–2.34)	1.51 (0.75–3.04)	**2.78 (1.20–6.43)**	1.47 (0.77–2.82)	1.05 (0.50–2.17)	2.84 (1.17–6.91)	1.43 (0.77–2.65)	1.85 (0.75–4.57)	1.09 (0.55–2.18)
Glaucoma, medication	1.26 (0.36–4.49)	0.50 (0.17–1.49)	0.84 (0.25–2.81)	0.47 (0.20–1.16)	0.44 (0.11–1.81)	0.62 (0.17–2.28)	0.98 (0.42–2.29)	0.85 (0.30–2.40)	0.46 (0.16–1.35)	0.90 (0.31–2.58)	0.53 (0.20–1.38)	1.52 (0.50–4.59)
Glaucoma, operated	0.42 (0.16–1.12)	0.15 (0.02–1.09)	0.53 (0.19–1.48)	2.06 (0.44–9.59)	0.10 (0.01–1.65)	0.83 (0.29–2.36)	0.48 (0.23–1.04)	0.40 (0.10–1.55)	0.64 (0.17–2.38)	0.61 (0.22–1.67)	0.68 (0.19–2.42)	0.82 (0.18–3.73)

The ORs and 95% confidence intervals were estimated through logistic regression analysis corrected for age, gender and the most common comorbidities. Bolded values denote statistically significant (p < 0.05) ORs. Verified, self-reported and self-suspected glaucoma patients were compared to glaucoma negatives (OR = 1.0), glaucoma patients with glaucoma medication to all glaucoma patients without glaucoma medication, and verified glaucoma patients who had undergone eye surgery due to the disease to all verified glaucoma patients who had not been operated.
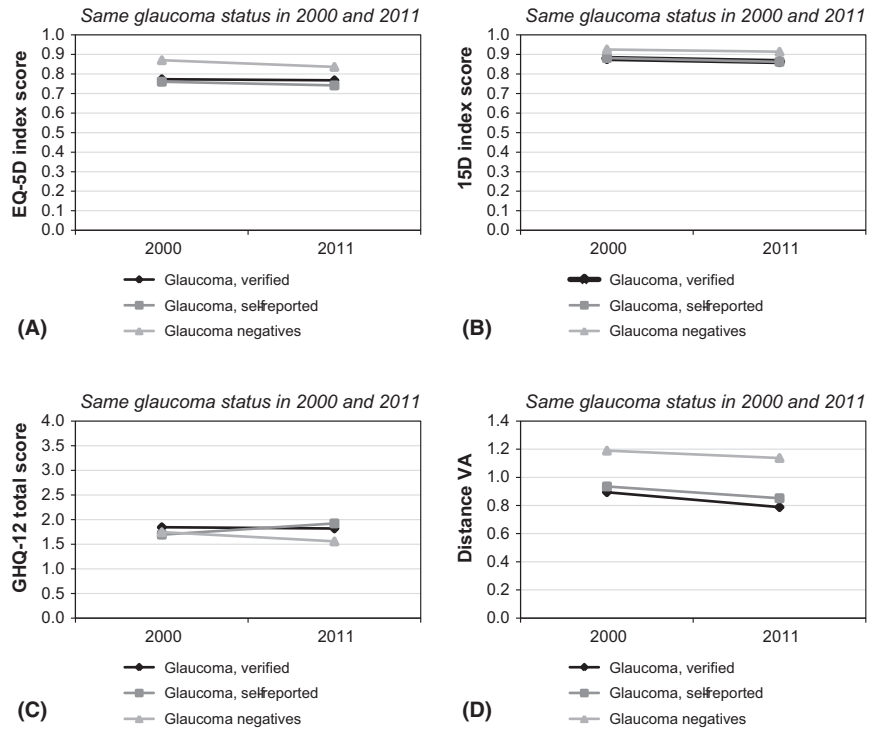
Fig. 4. Change in health-related quality of life (A, B), psychological distress (C) and distance visual acuity (VA; D) in glaucoma negatives and glaucoma patients with *the same glaucoma status* in both time points during the 11-year follow-up.
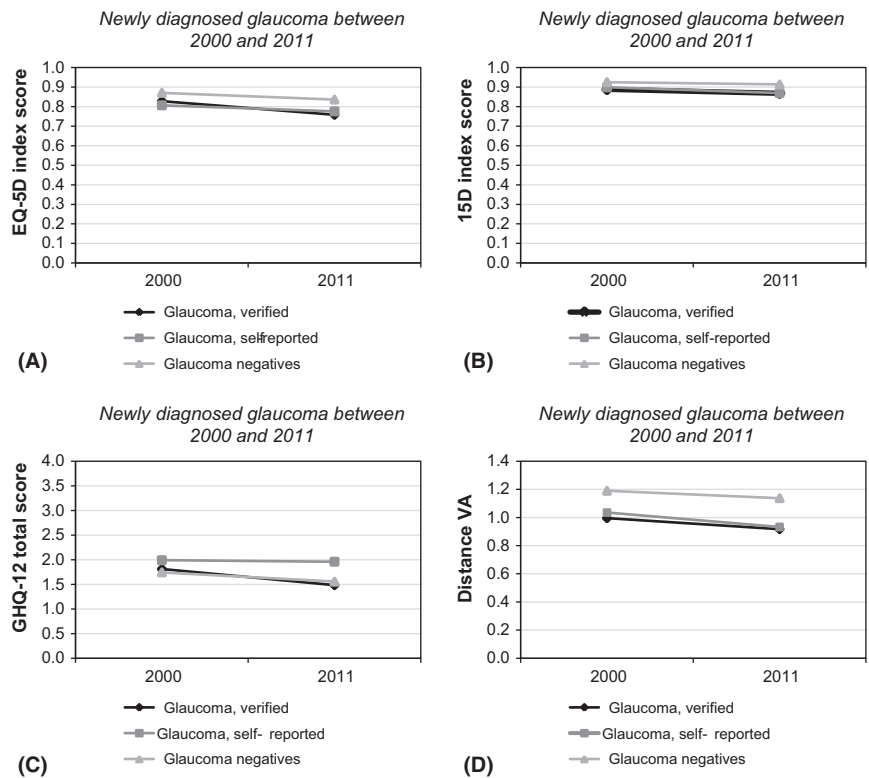
Fig. 5. Change in health-related quality of life (A, B), psychological distress (C) and distance visual acuity (VA; D) in individuals with *newly diagnosed glaucoma* (verified or self-reported) during the 11-year follow-up (2000–2011). Individuals with glaucoma negative status in both time points are shown as reference.

which have utilized vision-related HRQoL instruments (Floriani et al. 2016; Rulli et al. 2018; Machado et al. 2019; Wu et al. 2019). In our study, the mean score in these values was increasing between 2000–2011 in the cross-sectional setting, indicating an increase in the overall well-being and the potentially diminished role of glaucoma on generic HRQoL. As far as we know, this is the first time this type of effect of glaucoma has been reported using generic HRQoL instruments.

Worsening of mental health was more common amongst glaucoma patients and those who only suspected to have glaucoma based on significant worsening of the BDI scores compared to the non-glaucomatous population. Similar results were reported by Jung and co-workers (Jung & Park 2016), who found that undiagnosed glaucoma positives might be more depressed compared to non-glaucoma controls, even though the degree of depression may not be sufficient for a depression diagnosis. Patients with visual impairment and eye diseases, including glaucoma, have shown to have a higher probability of being depressed and having problems with anxiety/depression than healthy individuals (Popescu et al. 2012; Jung & Park 2016). In our study, the effect of visual impairment had a significantly stronger effect on BDI than glaucoma alone. Previous publications have suggested that the awareness of the eye disease itself may affect the sense of well-being in glaucoma patients because of the fear of declining vision (Jampel et al. 2007; Wang et al. 2012; Su et al. 2015). In our study, verified glaucoma patients also showed an increased prevalence of psychological distress as well as overall worsening of the GHQ-12 total score in 2000.

When investigating the individual dimensions of the used generic HRQoL instruments, all three glaucoma groups showed the most difficulties concerning usual activities, self-care, mobility and vision. These dimensions also showed an association with decreasing VA. Similar results were reported by Freeman and co-workers (Freeman et al. 2008), who implemented a vision-related HRQoL instrument and discovered that glaucoma affects mobility and increases difficulties in various visual tasks. In our study, worsening in the overall HRQoL and mental health also showed association with decreasing VA

in both glaucoma patients and glaucoma negatives, which supports the known association between decreased QoL and impaired vision (McKean-Cowdin et al. 2010; Quaranta et al. 2016). Jung and co-workers demonstrated that glaucoma may affect EQ-5D, especially in patients with reduced VA (Jung & Park 2016). The strong impact of visual impairment on HRQoL in this study supports our previous study, in which we used identical data set to identify declined VA as the major determinant in the decreased HRQoL in the most common eye diseases (Purola et al. 2021). However, as all glaucoma groups showed worsened scores in these parameters compared to glaucoma negatives, glaucoma and fear of it nonetheless can affect the common activities of life, and therefore HRQoL.

Medical treatment as such showed no significant difference in generic HRQoL or mental health amongst glaucoma patients. This is most probably because glaucoma treatment is potentially having both positive and negative effects on QoL (Quaranta et al. 2016). Glaucoma patients who had undergone eye surgery due to their disease showed increased odds for pain/discomfort and difficulties in the usual activities according to EQ-5D in 2000. No difference in HRQoL or mental health was found between operated and unoperated glaucoma patients in 2011. This parallels with results from Guedes et al. (2013), who found no significant difference between glaucoma patients treated with either surgery or medicine, and that glaucoma surgery is associated with a lower vision-related QoL only in patients with early glaucoma, possibly due to psychological burden. Moreover, Hyman and co-workers reported no difference in vision-related HRQoL between treated and untreated glaucoma patients in an EMGT-study (Hyman et al. 2005).

In the longitudinal setting, patients having glaucoma already at the beginning of follow-up did not show similar improvement in HRQoL during the 11-year follow-up that was found as in the cross-sectional comparison. In fact, a small decline in HRQoL was found in both glaucoma patients and glaucoma negatives who had the same eye status in both the time points, most probably related to ageing. Improvement in HRQoL in the cross-sectional setting could be explained by the fact that

newly diagnosed glaucoma during the 11 years had only a minor effect on generic HRQoL. Furthermore, no effect was observed in mental health with newly diagnosed glaucoma. This indicates that the decrease in the deteriorating effects of glaucoma on generic HRQoL and mental health is related to new glaucoma cases rather than the changes amongst those patients that have had glaucoma already in 2000. Riva and co-workers (Riva et al. 2019) reported improved vision-related QoL and reduction in glaucoma-related symptoms during their one-year follow-up study consisting of newly diagnosed primary open-angle glaucoma patients, and they suggested that it could be due to the patients' psychological processes and adaptation to the diagnosis.

The greatest strengths of our study were that our data were based on two nationwide surveys with high participation rates, and the loss between time points was relatively small and was further corrected by applying the weights. As most of the individuals participated in both the surveys, we were able to include a relatively long, 11-year longitudinal follow-up study. Furthermore, we used generic HRQoL instruments rather than vision-related instruments for better comparability and generalization of our results. Lastly, we were able to use comprehensive Finnish nationwide health registries when obtaining data from verified diagnoses, medical therapies and glaucoma surgeries.

However, our study also has potential limitations. As the number of different glaucoma diagnoses was relatively low, we could not account for differences between the various glaucoma types, and instead, we combined all glaucoma diagnoses into a single verified glaucoma group. For the same reasons, we did not account for the effects of various types of eye drops or surgeries on HRQoL. Both the surveys included predominantly Finnish participants, and therefore, the results may not be applicable to other countries and ethnicities. However, we used UK time-trade-off weights for EQ-5D, which may improve the comparability with other ethnicities.

In the future studies, more nationwide-based studies on glaucoma with generic HRQoL instruments and longitudinal settings of 10+ years could

improve the comparability and generalization of our results. Furthermore, full data on the different types of glaucoma and medication could make it possible to assess a more detailed effect of glaucoma treatment on HRQoL.

In conclusion, our results show that glaucoma as well as self-suspicion of it have a deteriorating impact on generic HRQoL and mental health. However, the impaired VA associated with glaucoma is stronger determinant of these parameters than the awareness or suspicion of the disease. Moreover, this deteriorating impact appears to be diminishing since the effects were less significant in 2011 than in 2000. This reflects merely the fact that newly diagnosed glaucoma during the 11-year follow-up seemed to have only a minor effect on the HRQoL and mental health rather than improvement in these parameters amongst old glaucoma patients. Treatment of glaucoma, neither the medication nor surgery, does not have significant effect on generic HRQoL or mental health.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Glaucoma groups in 2000 (A) and 2011 (B).

Figure S2. Association between health-related quality of life (A, B) and mental health (C, D) with distance visual acuity (VA) in verified and self-reported glaucoma patients, glaucoma negatives and glaucoma patients with known glaucoma medication in 2000.

Figure S3. Association between health-related quality of life (A, B) and mental health (C, D) with distance visual acuity (VA) in verified and self-reported glaucoma patients, glaucoma negatives and glaucoma patients with known glaucoma medication in 2011.

Figure S4. Individual EQ-5D dimensions and their association with distance visual acuity (VA) in verified and self-reported glaucoma patients, glaucoma negatives and glaucoma patients with known glaucoma medication in 2000

Figure S5. Individual 15D dimensions and their association with distance visual acuity (VA) in verified and self-reported glaucoma patients, glaucoma negatives and glaucoma patients with known glaucoma medication in 2000

Table S1. Estimated percentages of different glaucoma diagnoses in the Finnish population aged 30 years and older in 2000 and 2011.

Table S2. Linear regression analysis examining the impact of glaucoma on distance visual acuity with cataract and retinal degeneration (RD) as covariates in 2000 and 2011.