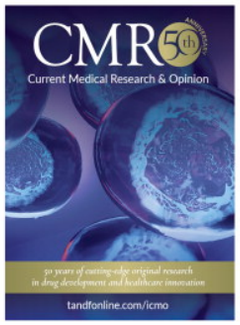

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RESEARCH ARTICLE

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Prevalence of comorbidities with the potential to increase the risk of nonadherence to topical ocular hypotensive medication in patients with open-angle glaucoma

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ABSTRACT

Objective: To evaluate the prevalence of comorbidities that may limit or prevent adherence to topical ocular hypotensive therapy in patients with open-angle glaucoma (OAG).

Methods: The UK Clinical Practice Research Datalink (CPRD) database of primary and secondary care and prescription records was analyzed to identify patients with a first (index) diagnosis of OAG during 2016–2020. The primary care records of these patients were screened for diagnostic terms linked to prespecified (qualifying) comorbidities considered to have the potential to impact patients' ability to instill eye drops. The prevalence of each of 10 categories of qualifying comorbidity recorded within the period from 5 years before to 2 years after the index OAG diagnosis was analyzed.

Results: A total of 100,968 patients with OAG were included in the analysis. Among the patients in the OAG cohort, 13,962 (13.8%) were aged 40–54 years, 32,145 (31.8%) were aged 55–69 years, 42,042 (41.6%) were aged 70–84 years, and 12,819 (12.7%) were aged 85+ years. Within the OAG population, 82.7%, 14.6%, and 2.7% of patients had no category, one category, and two or more categories of qualifying comorbidity, respectively. Qualifying comorbidities were most common in older patients. The most prevalent qualifying comorbidities were categorized as degenerative, traumatic, or pathological central nervous system disorder disrupting cognitive function (5.2%), movement disorder (4.4%), and low vision (4.1%). The prevalence of arthropathies and injuries affecting upper limbs (including arthritis in the hands) was 2.4%.

Conclusions: The presence of comorbidities should be considered when determining whether eye drops are suitable treatment for glaucoma. Neurodegenerative disease affecting cognition and memory, motor disease, and low vision are common comorbidities that may impact adherence to eye drops, and affected patients may benefit from non-drop treatment modalities.

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Adherence; comorbidity; dementia; electronic health records; eye drops; open-angle glaucoma

Introduction

Glaucoma is a progressive, degenerative disease of the optic nerve and the leading cause of irreversible blindness[1]. The most common form of glaucoma worldwide is open-angle glaucoma (OAG)[2], and primary OAG (POAG) is the most common type of OAG[3]. The main modifiable risk factor for the development and progression of OAG is intraocular pressure (IOP)[4–8]. Currently, all treatments for glaucoma aim to lower IOP.

Effective control of IOP has been demonstrated to slow visual field deterioration in OAG[9,10]. Because of the chronic nature of OAG, life-long IOP-lowering therapy is usually required. First-line treatment for OAG usually comprises topical IOP-lowering medication, with treatment often initiated in a stepwise fashion starting with single topical drug therapy (typically a prostaglandin analog), followed by multidrug combinations or laser therapy, and, if necessary, surgical interventions[11,12]. Alternatively, the current European Glaucoma Society (EGS) guidelines advise that selective laser trabeculoplasty (SLT) can be offered as an initial treatment, based on consideration of factors such as comorbidities, the ability to administer eye drops, patient preferences, cost, and availability[12]. Finally, in some cases where a lower target IOP is required, surgery could also be considered as a first-line option.

As with other chronic diseases, poor adherence of patients to daily medication is a major impediment to disease management in glaucoma. Although there is an

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established risk of progression to advanced disease, early stages of glaucoma are asymptomatic, and patients often do not understand the need to treat an asymptomatic disease[13]. Glaucoma patients' adherence (consistent daily use of medication in accordance with dosage recommendations) and persistence (continued use of medication over time) with IOP-lowering eye drops is typically poor[14–18]. Studies generally have indicated that some 30–80% of patients fail to adhere to their topical medication regimen[14,15,17]. Persistence with topical IOP-lowering medication is likewise suboptimal, with 20–86% of patients failing to continue on their initially prescribed treatment at 12 months[15,19]. In one study, among patients initiated on topical IOP-lowering therapy for confirmed or suspected glaucoma, nearly 50% were reported to have discontinued medication within the first 6 months, and only 37% filled their prescription at 3 years[20].

Despite evidence of overall efficacy, topical IOP-lowering treatment is not suitable for all patients. Patients may be unable to adhere strictly to their prescribed daily eye drop regimen or maintain continuous long-term treatment for a variety of reasons[13,17,21]. Some patients, particularly the frail and elderly, have problems when administering drops into the eye, such as instilling an inappropriate number of drops, missing the eye, or being unable to squeeze the bottle[22,23]. Observational studies have indicated that many glaucoma patients have difficulty instilling eye drops correctly, with 6.8–37.3% missing the eye with the drop, 11.3–60.6% not instilling exactly one drop, and 18.2–80% touching the tip of their eye drop bottle to the eye or face[22]. Factors associated with poor eye drop technique include advanced age, glaucoma-related visual impairment, and comorbidities such as arthritis[22,24,25].

Poor treatment adherence might be expected to contribute to suboptimal IOP control and, hence, to increased risk of glaucomatous damage and visual disability[26]. Findings from the topical medication arm of the Collaborative Initial Glaucoma Treatment Study (CIGTS), a prospective study that measured both medication adherence and visual fields, showed a statistically and clinically significant association between patients' self-reports of nonadherence during selected days of the study and glaucomatous vision loss over 8 years of follow-up[27]. The estimated mean loss in the visual field mean deviation (MD) was 0.62 dB in patients who reported missing no doses on any of the days, compared with 1.42 dB, 1.82 dB, and 2.23 dB in patients who reported missing doses on $\leq$1/3, 1/3–2/3, and $\geq$2/3 of the days, respectively (all $p < .001$). Additionally, a retrospective analysis of combined visual field and pharmacy data from Kaiser Permanente Southern California's HealthConnect electronic health record database showed a significant association between topical hypotensive medication nonadherence (based on the proportion of days covered by prescription fills and refills) and the rate of glaucomatous vision loss in clinical practice[28]. The estimated average annual loss in the visual field MD was 0.37 dB at a low (20%) adherence level compared with 0.32 dB at a high (80%) adherence level ($p = .006$)[28].

Multiple factors can adversely affect adherence to prescribed eye drops, such as forgetfulness, polypharmacy, inconvenience of drop administration (especially with multiple-drug regimens and medications requiring multiple drops per day), poor instillation technique, glaucoma-related vision loss, lack of knowledge about the long-term effects of glaucoma and the need for treatment, healthcare and medication costs, and side effects of the medication[17,29–31]. Among these side effects, signs and symptoms of dry eye (ocular surface disease [OSD]) occur in ~50% of medically treated OAG patients[32]. OSD is most prevalent in those receiving preserved eye drops and may discourage patients' continuation with therapy[33]. Other ocular side effects that may potentially discourage patients' adherence to ocular hypotensive medication include conjunctival hyperemia, deepening of the upper lid sulcus, and iris and periocular skin pigmentation with the topical prostaglandin analogs[34].

Non-drop treatment options to lower IOP in patients with OAG are ever-expanding, ranging from laser and incisional surgeries to the use of intracameral sustained-release drug implants[12,35]. The aim of this study was to help physicians identify patients at risk of nonadherence to IOP-lowering eye drops who may, therefore, benefit from non-drop treatment modalities. To this end, we evaluated the prevalence of comorbidities that are likely to affect adherence to eye drop therapy in patients with OAG.

Methods

This retrospective observational study was conducted using electronic health records (2014–2022) sourced from the Clinical Practice Research Datalink (CPRD), a comprehensive database of primary and secondary care and prescription records covering 13.3 million currently registered patients from 1,345 UK general practices (16.5% of all UK practices). CPRD comprises individual-level linked electronic records from primary care providers (including general practices, out-of-hours providers, and walk-in centers), community health providers, mental health services, and acute hospitals (including accident and emergency, inpatient, and outpatient episodes). The data accessed for the study were primary care records that do not include glaucoma-specific data such as intraocular pressure and visual field indices. In the UK healthcare system, the primary point of access for all initial diagnostic and secondary care referral purposes is the general practitioner. Specialized ophthalmology practices are not directly accessible to the patient; all access is referred through primary care, with details of ongoing care sent back to the general practitioner in the form of an update to the electronic medical record. The primary care records in the CPRD database consequently capture primary diagnoses and hospital attendances in addition to detailed records of any prescription drugs. Therefore, although detailed ophthalmological records are not available through the database, basic diagnostic data are reliably recorded. This gives considerable confidence that the OAG cohort identified is a fair representation of the underlying OAG population.

This study was approved by the Independent Scientific Advisory Committee of the Medicines and Healthcare products Regulatory Agency (protocol number: 23_002653). Informed consent was waived by the National Health Service Health Research Authority because individual patients cannot be identified from the database.

The database was screened to identify individuals with a first diagnosis of OAG documented in the period from 2016–2020, based on the presence of (i) a diagnostic Read code for OAG in the primary care record (Supplementary Table S1); or (ii) a procedural OPCS-4 Classification of Interventions and Procedures code for a glaucoma-specific procedure in the secondary care record (Supplementary Table S1); or (iii) a prescription record (British National Formulary code) for topical hypotensive medication (Supplementary Table S2). Patients were required to be aged ≥40 years at the time of the first diagnosis of OAG. Patients with a diagnostic Read code for ocular hypertension or a secondary or congenital glaucoma were excluded (Supplementary Table S3). The identified patients were stratified by gender and age, and the gender- and age-specific prevalence of OAG among patients aged ≥40 years in the database was determined.

The population of patients identified as having OAG was then screened for diagnostic terms in the primary care record (Read codes) linked to prespecified comorbidities considered to have the potential to impact patients' ability to instill eye drops. An international advisory board of ophthalmologists (listed in the Acknowledgements) selected the comorbidities included in the analysis, based on their medical experience and studies showing a relationship between the comorbidities and poor adherence to self-administration of eye drops[22–25,30,36,37]. The Read codes for these comorbidities are listed in Supplementary Table S4. The comorbidities were categorized as low vision; movement disorders (including congenital and degenerative central nervous system [CNS] disorders); post-stroke impairment and other paralyses; peripheral neuropathies and myopathies; arthropathies and injuries affecting the upper limbs; degenerative, traumatic, and pathological CNS disorders disrupting cognitive function; severe mental illness; substance dependence; intellectual disability; and CNS and mental conditions not otherwise specified (Table 1). The prevalence of each of the 10 individual categories of comorbidity, as well as the prevalence of comorbidities in multiple categories, were determined in patient cohorts stratified by gender and age.

Results

A total of 100,968 of 6,524,199 individuals (1.5%) in the database had an initial code for glaucoma (diagnosis or prescription) within the 5-year period of 2016–2020. Within this glaucoma population, 50,513 (50.0%) patients were male and 50,455 (50.0%) were female.

Among the glaucoma population, 17,497 (17.3%) patients had one or more qualifying comorbidity Read codes recorded either within the 5 years prior to their first

Table 1. Prespecified comorbidities with potential to decrease adherence to topical glaucoma medication.

Category	Description
1. Low vision	Visual impairment, poor visual acuity, vision loss, deteriorating vision, blindness
2. Movement disorders, including congenital and degenerative CNS disorders	Tics
	Movement disorders
	Essential tremor
	Hereditary and degenerative disease of the CNS (Parkinson's disease, amyotrophic lateral sclerosis, other movement disorders)
	Multiple sclerosis, paralysis, epilepsy, cerebral palsy
	Down's syndrome
3. Post-stroke impairment and other paralyses	Late effects of cerebrovascular disease
4. Peripheral neuropathies and myopathies	Mononeuritis of upper limb
	Hereditary and idiopathic peripheral neuropathy
	Inflammatory and toxic neuropathy
	Myoneural disorders, muscular dystrophy
	Systemic lupus erythematosus
	Polymyositis
5. Arthropathies and injuries affecting upper limbs	Crystal arthropathies in upper limbs
	Rheumatoid arthritis
	Osteoarthritis in upper limbs
	Joint derangement in upper limbs
	Joint disorder in upper limbs
	Reduction deformities of upper limb
6. Degenerative, traumatic, and pathological CNS disorders disrupting cognitive function	Dementia
	Other cerebral degenerations (including Alzheimer's disease)
	Dissociative amnesia
	Nonpsychotic mental disorder due to brain damage
	Anoxic brain damage
	Encephalopathy
7. Severe mental illness	Severe depression
	Psychosis
8. Substance dependence	Alcohol dependence
	Drug dependence
9. Intellectual disability	Mental retardation
10. CNS and mental conditions not otherwise specified	Physiological (musculoskeletal) malfunction arising from mental factors
	Other CNS disorders

Abbreviation. CNS, central nervous system.

Table 2. Number and percentage of glaucoma patients with no qualifying comorbidity or comorbidities in one or more categories.

Glaucoma cohort by age and gender	*N*	Patients with no comorbidity *n* (%)	Patients with comorbidity in only one category *n* (%)	Patients with comorbidity in two or more categories *n* (%)
Male				
40–54 years	7,756	6,897 (88.9)	756 (9.7)	103 (1.3)
55–69 years	16,884	14,793 (87.6)	1,846 (10.9)	245 (1.5)
70–84 years	20,650	16,721 (81.0)	3,245 (15.7)	684 (3.3)
85+ years	5,223	3,596 (68.8)	1,297 (24.8)	330 (6.3)
Female				
40–54 years	6,206	5,541 (89.3)	590 (9.5)	75 (1.2)
55–69 years	15,261	13,503 (88.5)	1,542 (10.1)	216 (1.4)
70–84 years	21,392	17,396 (81.3)	3,390 (15.8)	606 (2.8)
85+ years	7,596	5,024 (66.1)	2,070 (27.3)	502 (6.6)
Total population	100,968	83,471 (82.7)	14,736 (14.6)	2,761 (2.7)

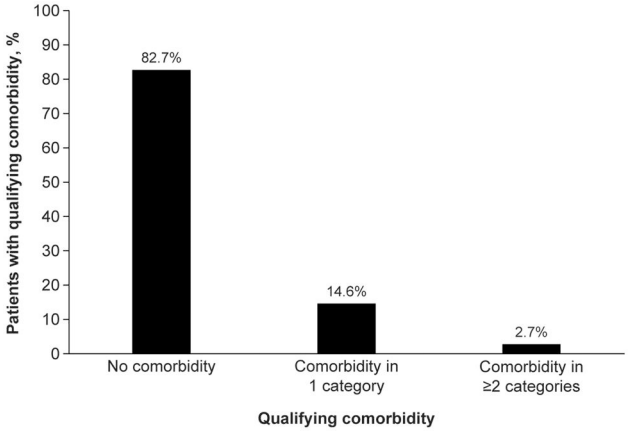

Figure 1. Prevalence of qualifying comorbidities within the glaucoma population.

glaucoma diagnosis or within 2 years following their initial glaucoma code. The prevalence of comorbidities was highest in the older age groups (Table 2). The proportion of patients with one or more categories of comorbidity was 10.9% for patients aged 40–54 years, 12.0% for patients aged 55–69 years, 18.9% for patients aged 70–84 years, and 32.8% for patients aged 85+ years (age group effect $p < .001$, Chi square test). For the majority of patients with comorbidities, all comorbidities fell within just one comorbidity category (Figure 1).

Table 3 shows the prevalence of the various types of qualifying comorbidity in the patients overall and in subgroups by age and gender. There was no clear effect of gender on the prevalence of comorbidities (Table 3). In both male and female patients, the most common qualifying comorbidities were degenerative, traumatic, and pathological CNS disorders disrupting cognitive function (category 6). As expected because of the inclusion of Alzheimer's disease and other age-related dementias in this comorbidity category, the prevalence of these comorbidities was strongly age-related and highest in patients aged ≥70 years (Table 3).

Movement disorders including congenital and degenerative CNS disorders (category 2) and low vision (category 1) were the next most prevalent qualifying comorbidities (Figure 2). Overall, 5.2% of patients had a degenerative, traumatic, or pathological CNS disorder disrupting cognitive function; 4.4% had a movement disorder; and 4.1% had low vision. Approximately 70% of the patients with a comorbidity in each of these three categories had no comorbidity in another category, whereas 30% also had a coexisting comorbidity in another category.

The pattern of prevalence of the different types of qualifying comorbidities was similar in patients who had just one category of qualifying comorbidity (Table 4).

Discussion

The results of this study suggest that patients who are at higher risk of nonadherence because of comorbidities tend to be older, with neurodegenerative disease affecting cognition and memory or with motor disease or low vision.

It is widely accepted that comorbidities can affect patient adherence to treatment in glaucoma[38]. In this study, we quantified the proportion of patients with OAG who, because of comorbidities, may potentially have problems with adhering to topical ocular hypotensive medication. The study design required an initial glaucoma diagnosis in the index period from 2016–2020 so that patients in the early years of their glaucoma diagnosis, who are most likely to be treated with topical medication, would be identified. Identification of the target patient group was dependent on the original disease coding used by the clinician at the time of patient coding. Although patients with codes explicitly identifying a diagnosis of congenital glaucoma or secondary glaucoma were excluded, in many cases a non-specific OAG code was documented. Therefore, the source population for this analysis should be considered a mixed population of patients aged ≥40 years with POAG and secondary OAG.

The most common category of comorbidity potentially associated with decreased adherence in the glaucoma population was degenerative, traumatic, and pathological CNS disorders disrupting cognitive function. Consistent with this finding, the most common reason for nonadherence in glaucoma patients has been reported to be memory problems or forgetfulness[17,39]. Moreover, the risk of Alzheimer's disease and other dementias is increased in glaucoma[40,41], yet results from a large population-based study in Australia suggested that individuals with Alzheimer's disease are less likely to receive medication for glaucoma compared with age- and gender-matched controls[42]. Taken together, study results

Table 3. Number and percentage of glaucoma patients with each category of comorbidity.

Glaucoma cohort by age and gender	*N*	Comorbidity category, *n* (%)									
		1	2	3	4	5	6	7	8	9	10
Male											
40–54 years	7,756	265 (3.4)	223 (2.9)	8 (0.1)	93 (1.2)	43 (0.6)	16 (0.2)	111 (1.4)	207 (2.7)	9 (0.1)	<5 (<0.06)
55–69 years	16,884	509 (3.0)	581 (3.4)	22 (0.1)	279 (1.7)	291 (1.7)	156 (0.9)	182 (1.1)	318 (1.9)	8 (0.05)	28 (0.2)
70–84 years	20,650	815 (3.9)	1,176 (5.7)	50 (0.2)	470 (2.3)	486 (2.4)	1,333 (6.5)	121 (0.6)	162 (0.8)	7 (0.03)	151 (0.73)
85+ years	5,223	450 (8.6)	325 (6.2)	<5 (<0.1)	117 (2.2)	110 (2.1)	873 (16.7)	21 (0.4)	14 (0.3)	0 (0)	92 (1.8)
Female											
40–54 years	6,206	176 (2.8)	200 (3.2)	<5 (<0.08)	65 (1.0)	60 (1.0)	10 (0.2)	108 (1.7)	116 (1.9)	<5 (<0.08)	<5 (<0.08)
55–69 years	15,261	402 (2.6)	506 (3.3)	14 (0.09)	184 (1.2)	398 (2.6)	113 (0.7)	204 (1.3)	162 (1.1)	<5 (<0.03)	11 (0.07)
70–84 years	21,392	780 (3.6)	1,059 (5.0)	31 (0.1)	324 (1.5)	785 (3.7)	1,343 (6.3)	165 (0.8)	91 (0.4)	<5 (<0.02)	127 (0.6)
85+ years	7,596	704 (9.3)	374 (4.9)	7 (0.09)	116 (1.5)	284 (3.7)	1,435 (18.9)	62 (0.8)	15 (0.2)	0 (0)	143 (1.9)
Male, %		4.0	4.6	0.2	1.9	1.8	4.7	0.9	1.4	0.05	0.5
Female, %		4.1	4.2	0.1	1.4	3.0	5.7	1.1	0.8	0.03	0.6
p value*		.935	.442	.939	.409	.071	.093	.741	.356	.962	.975

Values of 1–4 are reported as <5 to preserve patient anonymity.
**p* value for prevalence in males vs females based on Chi square test.

suggest that patients with glaucoma and Alzheimer's disease or other dementia are poor candidates for topical glaucoma treatment[17,39,42,43].

The next most prevalent qualifying comorbidities in the glaucoma population were movement disorders and low vision. Tremor has been shown to be associated with unsuccessful self-administration of drops by glaucoma patients[24], and the movement disorders comorbidity category included essential tremor as well as Parkinson's disease and multiple sclerosis, which are commonly associated with hand tremor. Ataxia was also included in the movement disorders category and has been demonstrated to be a significant risk factor for instillation failure[23].

Studies have also shown that glaucomatous visual field loss is associated with a decreased ability of glaucoma patients to successfully instill eye drops[22,23]. The comorbidity category of low vision used in the present analysis included 87 disease codes. Most of these codes describe visual impairment, poor visual acuity, vision loss, low vision, deteriorating vision, or blindness of unspecified cause. Low vision was included in the analysis because it is a condition that can affect adherence to eye drops, regardless of whether it occurs as a sequelae in advanced glaucoma or for other reasons. In some cases, the low vision potentially could have been related to a reversible cause such as cataract and, when recorded during the 5 years before the first glaucoma diagnosis, may not have persisted after the glaucoma diagnosis.

The prevalence of category 5 comorbidities (including arthritis in the hands) was lower, but this type of comorbidity may be particularly important in causing nonadherence because of patients not being able to accurately instill a single drop in the eye. Studies evaluating eye drop instillation technique in patients with glaucoma have shown an association between arthritis and the inability to place a drop in the eye[24,25]. Further, a study evaluating eye drop instillation in a rheumatoid arthritis population demonstrated that people with rheumatoid arthritis have difficulty instilling eye drops[44].

These comorbidities would not be expected to limit adherence in patients who have a caregiver responsible for remembering to use the drops and administering them as prescribed. The proportion of glaucoma patients on drops who have assistance in instilling the drops (i.e. a partner or caregiver puts the drop in the eye) is unknown. However, in a large study in glaucoma patients seen in primary care clinics in Israel, 23% (168/714) of the patients reported having help from a family member or other caregiver in administering their drops[45].

All IOP-lowering drops have associated side effects, and these side effects can lead to decisions to switch treatments[46]. In a recent survey of 783 patients with glaucoma, 6.3% of patients were dissatisfied or very dissatisfied with the tolerability of their existing eye drops[47]. However, studies of patient preferences in glaucoma management generally have indicated that patients value attributes of their drops such as effectiveness in IOP lowering and convenience more than comfort[48], and side effects are not a primary reason for nonadherence[17,49]. Results of studies of self-reported adherence and reasons for nonadherence generally have reported that nonintentional nonadherence (e.g. because of forgetfulness or drops missing the eye) is much more common than intentional nonadherence (e.g. because of side effects), especially for patients who are educated on the importance of adhering to treatment to reduce the risk of vision loss[17,49,50]. The proportion of patients who stop using their drops or skip doses because of side effects has not been well investigated. Nonetheless, side effects have been identified as a barrier to adherence[51]. In a study of 201 patients with glaucoma, the self-reported rate of nonadherence was twice as high (37.6%) in patients who reported side effects of

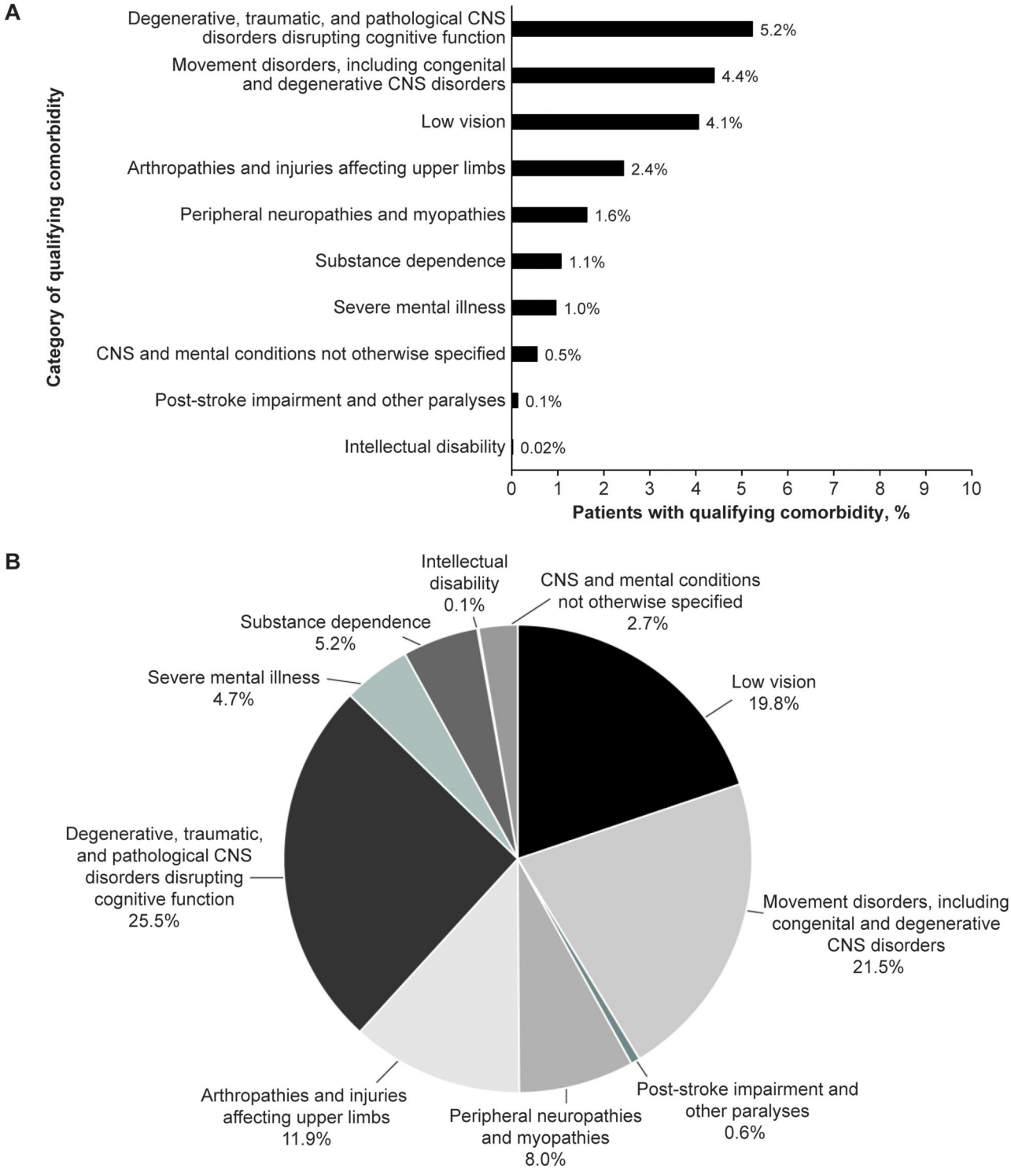

Figure 2. Prevalence of qualifying comorbidities within the glaucoma population. (a) Proportion of OAG patients with each category of comorbidity. (b) Proportion of qualifying comorbidities by category within the OAG population. Abbreviations: CNS, central nervous system; OAG, open-angle glaucoma.

treatment compared with those who reported no side effects (18.4%)[52].

There are several limitations of this analysis. The study design did not include a control comparator group. Also, we determined the prevalence of qualifying comorbidities in the OAG population, but the relationship between these comorbidities and adherence was not evaluated. Many factors may contribute to the risk of nonadherence for an individual glaucoma patient, and comorbidities are just one of those factors. Factors other than comorbidities that could make patients unsuitable for topical glaucoma treatment, such as side effects including OSD, were not captured in this analysis. Also, the presence of a qualifying comorbidity does not necessarily indicate that a patient will be nonadherent to drops. For some comorbidities, the risk of nonadherence may be related to disease severity, which was not captured by the disease

Table 4. Distribution of glaucoma patients with comorbidities in only one category.

Glaucoma cohort by age and gender	Patients with one category of comorbidity, *N*	Comorbidity category, *n* (%)									
		1	2	3	4	5	6	7	8	9	10
Male											
40–54 years	756	210 (27.8)	177 (23.4)	<5 (<0.7)	63 (8.3)	32 (4.2)	7 (0.9)	86 (11.4)	172 (22.8)	<5 (<0.7)	<5 (<0.7)
55–69 years	1,846	403 (21.8)	451 (24.4)	10 (0.5)	228 (12.4)	254 (13.8)	95 (5.1)	136 (7.4)	260 (14.1)	5 (0.3)	<5 (<0.3)
70–84 years	3,245	556 (17.1)	812 (25.0)	25 (0.8)	341 (10.5)	398 (12.3)	894 (27.6)	73 (2.2)	111 (3.4)	<5 (<0.2)	34 (1.0)
85+ years	1,297	315 (24.3)	187 (14.4)	<5 (<0.4)	66 (5.1)	76 (5.9)	614 (47.3)	9 (0.7)	6 (0.5)	0 (0)	22 (1.7)
Female											
40–54 years	590	146 (24.7)	166 (28.1)	0 (0)	45 (7.6)	50 (8.5)	<5 (<0.8)	83 (14.1)	93 (15.8)	<5 (<0.8)	<5 (<0.8)
55–69 years	1,542	309 (20.0)	397 (25.7)	8 (0.5)	138 (8.9)	355 (23.0)	69 (4.5)	149 (9.7)	113 (7.3)	<5 (<0.3)	<5 (<0.3)
70–84 years	3,390	550 (16.2)	784 (23.1)	15 (0.4)	225 (6.6)	627 (18.5)	960 (28.3)	120 (3.5)	73 (2.2)	<5 (<0.1)	35 (1.0)
85+ years	2,070	460 (22.2)	198 (9.6)	<5 (<0.2)	77 (3.7)	200 (9.7)	1,058 (51.1)	29 (1.4)	8 (0.4)	0 (0)	37 (1.8)
Overall	14,736	2,949 (20.0)	3,172 (21.5)	66 (0.4)	1,183 (8.0)	1,992 (13.5)	3,700 (25.1)	685 (4.6)	836 (5.7)	14 (0.1)	139 (0.9)
% of total OAG population		2.9	3.1	0.07	1.8	2.0	3.7	0.7	0.8	0.01	0.1

Values of 1–4 are reported as <5 to preserve patient anonymity.
Abbreviation. OAG, open-angle glaucoma.

codes. For example, the severity of arthritis and level of incapacity associated with the disease could have significant consequences on the quality of instillation technique. Additionally, within the category of movement disorders including neurodegenerative CNS disease, the barrier to adherence is likely much higher for patients with Parkinsonian tremors compared with patients with controlled epilepsy. Furthermore, because many disease codes for movement disorders do not specify the affected limbs, movement disorders not affecting the upper limbs (which would be unlikely to affect adherence) could be included as qualifying comorbidities. Finally, patient comorbidities are relevant for patient self-administration of drops, but not when a caregiver administers the drops. Taking these limitations into consideration, we estimate that comorbidities may preclude adherence to topical ocular hypotensive medication in approximately 5–10% of patients with OAG and suggest that alternative non-drop modalities should be considered for this population.

Conclusions

Comorbidities such as dementia, depression, low vision, Parkinson's disease, and arthritis can impact the ability of patients to self-manage their glaucoma. Therefore, it is important for providers to ask patients whether they have difficulties and assistance in instilling eye drops. The presence of comorbidities should be considered when determining whether eye drops are suitable treatment or an alternative treatment should be used.

Transparency

Declaration of funding

AbbVie funded this study and participated in the study design; data interpretation; and the preparation, review, and approval of the manuscript.

Declaration of financial/other relationships

MFC is a consultant/contractor for Novartis, Théa, and Viatris; has received research support from Alcon and Théa; has received other financial compensation from AbbVie and Roche; and is an investor in Novai. PD is a consultant for AbbVie, Alcon, Horus, Santen, and Théa. CA and MR are employees of AbbVie and may hold stock. JB is a consultant for AbbVie. JGF is a consultant for AbbVie, Alcon, Alimera, Elios Vision, Glaukos Corp, iSTAR, Santen, and Théa; and has received research support from AbbVie, AJL Ophthalmic, Alcon, Bausch + Lomb, Glaukos Corp, Heidelberg Engineering, iSTAR, Johnson & Johnson, Pfizer, Santen, Sight Science, Théa, and ZEISS. Peer reviewers on this manuscript have received an honorarium from CMRO for their review work but have no other relevant financial relationships to disclose.

Author contributions

Study conception and design: JB, MR. Analysis and interpretation of the data: MFC, PD, CA, JB, MR, JGF. Drafting the manuscript and revising it critically for intellectual content: MFC, PD, CA, JB, MR, JGF. Final approval of the version to be published: MFC, PD, CA, JB, MR, JGF. All authors agree to be accountable for all aspects of this work.

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