

# Laser in Glaucoma and Ocular Hypertension Trial (LIGHT) in China – A Randomized Controlled Trial: Design and Baseline Characteristics



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- **PURPOSE:** To describe the baseline characteristics of a trial to evaluate whether selective laser trabeculoplasty (SLT), as a first-line treatment, provides superior economic and health-related quality of life outcomes to medical treatment in China.
- **DESIGN:** The LiGHT China trial is an unmasked, single-center, pragmatic, randomized controlled trial.
- **METHODS:** A total of 771 previously undiagnosed patients with primary open angle glaucoma (POAG, 622 patients) or ocular hypertension (OHT, 149 patients) at Zhongshan Ophthalmic Center were recruited from March 2015 to January 2019. Subjects were randomized to SLT-1st (followed by medication then surgery when required) or Medicine-1st (medication followed by surgery when required). The primary outcome was health-related quality of life (HRQL). The secondary outcomes were clinical outcomes, cost, cost-effectiveness, Glaucoma Utility Index, Glaucoma Symptom Scale, visual function, and safety.
- **RESULTS:** The mean age of POAG patients was 49.8 years and 38.8 years for OHT. The median intraocular pressure was 20 mm Hg for the 1,105 POAG eyes and 24 mm Hg for the 271 OHT eyes. POAG eyes had thin-

ner central cornea thickness (CCT, 536  $\mu\text{m}$ ) than OHT eyes (545  $\mu\text{m}$ ). Median mean deviation of the visual field in POAG eyes was -4.2 dB. Median refractive error was -1.5 D for OHT eyes and -1.25 D for POAG eyes. There was no difference between POAG and OHT patients on baseline scores of GUI, GSS and VF-14. The difference between OHT and POAG on the EQ-5D-5L was 0.024.

- **CONCLUSIONS:** Compared with participants in the LiGHT UK trial, participants in this trial were younger, more myopic and had more severe visual field defects. (Am J Ophthalmol 2021;230: 143–150. © 2021 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>))

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## INTRODUCTION

GLAUCOMA IS THE LEADING CAUSE OF IRREVERSIBLE blindness<sup>1</sup> and a major public health issue worldwide.<sup>2</sup> The prevalence of primary open angle glaucoma (POAG) is highest in African descent, followed by Asian and white patients.<sup>3</sup> In China, 13.12 million patients, who constitute 2.58% of the general population, were suffering from glaucoma in 2015. The prevalence is expected to increase to 3.48%, with 25.16 million people diagnosed as having glaucoma in China by 2050.<sup>4</sup> The overall prevalence of POAG in China ranges 0.7%-2.85%.<sup>4,5-8</sup> The already huge health burden from glaucoma in China will increase with the aging population, with a concurrent rise in costs. Up until now there are no prevalence data available for patients with ocular hypertension (OHT) from stringently designed prevalence studies in China.

The financial cost of POAG and OHT has been reported to be substantial in many countries, including Australia,<sup>9</sup> the UK,<sup>10</sup> Canada,<sup>11</sup> and the USA.<sup>12,13</sup> However, no relevant data are available to estimate the cost of glaucoma

treatment and the health-related quality of life (HRQL) of glaucoma patients in China. Considering the differences in socioeconomic studies, lifestyle and access to health care with other countries, extrapolation from these other sources may not be applicable to the Chinese population.

The Laser in Glaucoma and Ocular Hypertension (LiGHT) trial was conducted in the UK to compare the HRQL in patients with selective laser trabeculoplasty (SLT) or medication as first-line treatment for POAG and OHT.<sup>14,15</sup> The LiGHT UK trial found that SLT should be offered as a first-line treatment for POAG and OHT,<sup>16,17</sup> with a significant 3-year cost saving. In China, medication currently serves as the mainstream first-line treatment for POAG and OHT.<sup>18</sup> Studies in China<sup>19,20</sup> and other countries<sup>21-23</sup> have reported greatly varied treatment efficacy for SLT, which is possibly due to differences in severity of glaucoma, ethnic background,<sup>24,25</sup> laser energy used, treatment area, and length of follow-up. In the past, SLT has mainly been used for cases with uncontrolled intraocular pressure (IOP), intolerance to medical therapy and poor compliance in mild POAG.<sup>26-28</sup>

LiGHT China was an unmasked, single-center, pragmatic, randomized controlled trial aiming to compare HRQL in patients who were first treated with SLT with those treated with topical medication alone for newly diagnosed POAG and OHT. Pathway cost, cost-effectiveness and pathway effectiveness were secondary outcomes. This study mirrored the LiGHT Trial in UK,<sup>14</sup> with adaptations made to allow for the local medical practice framework in China.

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## METHODS

The study was approved by the ethical committees of Zhongshan Ophthalmic Center, Sun Yat-sen University and University College London, and informed consent was obtained from every patient before participation in the study. Consecutive eligible patients were recruited at Zhongshan Ophthalmic Center from January 2015 until January 2019. The study screened patients who were newly diagnosed in Zhongshan Ophthalmic Center and glaucoma/OHT suspects from nine other referral centers (Appendix 1) in Guangdong province. An eligibility exception was allowed for newly diagnosed patients who had initially been medically treated for up to 4 weeks; they underwent a 4-week washout period to obtain an untreated baseline pressure.<sup>14</sup> Patients treated with prostaglandins within 4 weeks before recruitment were excluded due to possible interaction with the mechanism of SLT. Patients who underwent cataract surgery more than 3 months before enrolment to the trial were eligible.

The methods (Appendix 2) used in disease definition, outcome measures and statistical analysis were consistent with the LiGHT UK trial.<sup>14</sup> All measurements affecting

treatment escalation decisions (visual field, optic disc imaging and IOP) were performed by observers blinded to treatment assignment. In the Laser-1<sup>st</sup> group, one SLT retreatment was allowed if there was an initial response to treatment. Cases failing to adequately respond to two SLT treatments were given medical treatment. The class of drugs as first-line, second-line or third-line was defined by NICE<sup>29</sup> and European Glaucoma Society guidance.<sup>30</sup>

The primary outcome was HRQL at 3 years, assessed by EuroQol EQ-5D-5 Levels (EQ-5D-5L). The utility scores of EQ-5D-5L were calculated using Chinese<sup>31</sup> and English time-tradeoff value sets,<sup>32</sup> respectively. Except for using Visual Function-14 (VF-14) instead of Glaucoma Quality of Life-15 (GQL-15), the other secondary outcome measurements were the same as the LiGHT UK project, including treatment pathway cost, cost-effectiveness, Glaucoma Utility Index (GUI), Glaucoma Symptom Scale (GSS), objective measure of pathway effectiveness and safety profiles, as well as compliance. All of the adjustments were made in accordance with China's national conditions (Appendix 2).

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## RESULTS

• **BASELINE PATIENT CHARACTERISTICS:** A total of 1,376 eyes of 771 participants were included in the study: 483 (62.6%) patients had bilateral POAG and 139 (18.1%) had unilateral POAG (fellow eye healthy); 122 (15.8%) had bilateral OHT and 27 (3.5%) had unilateral OHT. A total of 622 participants (80.7%) were classified as POAG and 149 (19.3%) were classified as OHT. Of the participants: 581 accepted phasing (24-hour IOP monitoring) bilaterally, 87 accepted phasing only for the left eye and 71 only for the right eye (Table 1 summarizes the baseline patient characteristics).

There were 72 males (48.3%) and 77 females (51.7%) in OHT patients, while POAG patients comprised 364 males (58.5%) and 258 females (41.5%). The mean age for patients diagnosed with POAG was 49.8 years (SD = 17.2 years) and OHT 38.8 years (SD = 14.7 years). On average, the LiGHT China cohort was significantly younger compared with the LiGHT UK cohort (OHT: mean LiGHT China 38.8 years vs LiGHT UK 58 years; POAG: mean LiGHT China 49.8 years vs LiGHT UK 64 years). Sixty-nine (11%) patients with POAG reported a family history of glaucoma compared with 15 (10%) in the OHT group. The prevalence of systemic hypertension and diabetes was lower in the LiGHT China cohort than in LiGHT UK. Notably, nobody was diagnosed with Raynaud's syndrome in the current cohort. There were 157 (25.2%) tobacco users or ex-smokers in the POAG and 39 (26.2%) in the OHT patients. Ninety-four (15.1%) POAG patients were alcohol users and there were 21 (14.1%) in the OHT group. In both groups, the recruited patients with professional occupations (engineers, nurses, doctors, etc.) accounted for the

**TABLE 1.** Baseline characteristics of participants in LiGHT UK versus LiGHT China

		LiGHT UK N (%)		LiGHT China N (%)		
		OHT (n = 163)	POAG (n = 555)	OHT (n = 149)	POAG (n = 622)	
<b>Total number</b>		163 (22.7)	555 (77.3)	149 (19.3)	622 (80.7)	
<b>Affected Eye (s)</b>	<b>Unilateral</b>	39 (5.4)	254 (35.4)	27 (3.5)	139 (18.1)	
	<b>Bilateral</b>	124 (17.3)	301 (41.9)	122 (15.8)	483 (62.6)	
<b>Eligibility</b>	<b>Right eye</b>	96 (13.4)		73 (9.5)		
	<b>Left eye</b>	104 (14.5)		93 (12.0)		
	<b>Bilateral</b>	518 (72.1)		605 (78.5)		
<b>Gender</b>	<b>Male</b>	94 (58)	303 (55)	72 (48)	364 (59)	
	<b>Female</b>	69 (42)	252 (45)	77 (52)	258 (41)	
<b>Age</b>	<b>Mean (SD)</b>	58 (11)	64 (12)	39 (15)	50 (17)	
<b>General health</b>	<b>Asthma</b>	17 (10)	76 (14)	1 (1)	6 (1)	
	<b>Hypertension</b>	60 (37)	191 (34)	14 (9)	111 (18)	
	<b>Diabetes</b>	24 (15)	58 (10)	5 (3)	30 (5)	
	<b>Angina</b>	4 (2)	17 (3)	1 (1)	9 (1)	
	<b>Cardiac arrhythmia</b>	4 (2)	33 (6)	4 (3)	18 (3)	
	<b>Ischemic heart disease</b>	3 (2)	17 (3)	0 (0)	19 (3)	
	<b>Migraines</b>	16 (10)	78 (14)	2 (1)	3 (0.5)	
	<b>Cerebrovascular accident or stroke</b>	2 (1)	12 (2)	1 (1)	1 (0.2)	
	<b>Peripheral vasospastic symptoms</b>	7 (4)	56 (10)	0 (0)	0 (0)	
	<b>Blood loss or transfusion</b>	14 (9)	62 (11)	1 (1)	3 (0.5)	
	<b>Family history of glaucoma</b>		46 (28)	168 (30)	15 (10)	69 (11)
	<b>Smoker<sup>a</sup></b>		-	-	26 (17)	83 (13)
	<b>Drinker<sup>b</sup></b>		NA	NA	21 (13)	94 (15)

NA = not acquired, OHT = ocular hypertension, POAG = primary open angle glaucoma

<sup>a</sup>11% of all included patients were smokers in LiGHT UK

<sup>b</sup>The proportion of drinkers was not reported in LiGHT UK

**TABLE 2.** Baseline intraocular pressure (IOP) in the two diagnostic groups

Diagnosis	Severity classification	N (%)	IOP (mm Hg)Mean ± SD	IOP (mm Hg)Median (IQR)
<b>OHT</b>		271 (19.7%)	24.43 ± 3.17	24 (22-26)
<b>POAG</b>		1,105 (80.3%)	20.36 ± 5.40	20 (17-23)
	<b>Mild POAG</b>	684 (49.7%)	20.29 ± 5.11	20 (17-23)
	<b>Mod POAG</b>	304 (22.1%)	20.73 ± 5.87	20 (17-23)
	<b>Severe POAG</b>	117 (8.5%)	19.78 ± 5.80	19 (16.5-23)

OHT = ocular hypertension, POAG = primary open angle glaucoma

largest proportion: 182 (29.3%) for POAG and 34 (22.8%) for OHT groups (Table 1).

• **BASELINE CHARACTERISTICS FOR ELIGIBLE EYES:** A total of 1,105 eyes (80.3%) were classified as POAG and 271 eyes (19.7%) were defined as OHT. The median IOP for OHT eyes was 24 mm Hg and 20 mm Hg for POAG eyes. The baseline IOP of OHT eyes was significantly higher than that of POAG eyes ( $P < .001$ ), while no significant difference was found between the baseline IOP of POAG subgroups (mild, moderate and severe POAG) ( $P = .221$ ) (Table 2). Mean central corneal thickness (CCT) was 536  $\mu\text{m}$  for POAG eyes and 545  $\mu\text{m}$  for OHT eyes. POAG eyes

had thinner CCT than OHT eyes, with statistical significance ( $P < .001$ ). However, after grouping both POAG and OHT eyes with ranges of CCT, there was no statistical difference in the proportion of eyes with CCT  $< 500 \mu\text{m}$  between the two groups (11.5% in POAG vs 7.7% in OHT, Chi-square test  $P = .205$ ) (Table 3). Median VF MD for OHT and POAG eyes was -1.53 dB and -4.23 dB, respectively. Median neuroretinal rim area was 1.14  $\text{mm}^2$  for POAG eyes and 1.36  $\text{mm}^2$  for OHT eyes (Table 4).

Median refractive error was -1.5 D in the POAG group and -1.25 D in the OHT group. In both groups, myopia accounted for the majority (OHT: 73.8%; POAG: 67.8%), of which mild myopia had the highest proportion. A sig-

**TABLE 3.** Distribution of central corneal thickness in the two diagnostic groups

Diagnosis	Variables	Mean ± SD (μm)		N (%)
<b>OHT</b>	<b>CCT (μm)</b>	544.64 ± 29.13	< 500	21 (7.7%)
			500-554	173 (63.8%)
			555-590	58 (21.4%)
			> 590	19 (7.0%)
<b>POAG</b>	<b>CCT (μm)</b>	536.08 ± 33.54	< 500	127 (11.5%)
			500-554	658 (59.5%)
			555-590	258 (23.3%)
			> 590	62 (5.6%)

CCT = central corneal thickness, OHT = ocular hypertension, POAG = primary open angle glaucoma

**TABLE 4.** Baseline of included eyes in LiGHT UK vs LiGHT China

	UK		China	
	OHT (n = 380)	POAG (n = 854)	OHT (n = 271)	POAG (n = 1,105)
<b>Refractive error, (Spherical D), median (IQR)</b>	0.44 (-0.75 to 1.5)	0.25 (-1.5 to 1.5)	-1.5 (-5 to 0)	-1.25 (-4.5 to 0.5)
<b>Myopia<sup>a</sup>, eyes (%)</b>	<b>High</b>	NA	66 (24)	213 (19)
	<b>Moderate</b>	NA	52 (19)	231 (21)
	<b>Low</b>	NA	82 (30)	305 (28)
<b>Hyperopia, eyes (%)</b>	NA	NA	31 (11)	220 (20)
<b>Visual acuity, median (IQR)</b>	0.02 (-0.08 to 0.12)	0.06 (-0.02 to 0.16)	0.14 (0 to 0.3)	0.2 (0.02 to 0.4)
<b>IOP, median (IQR)</b>	26 (24 to 29)	23 (20 to 27)	24 (22 to 26)	20 (17 to 23)
<b>VF MD (dB), median (IQR)</b>	-0.81 (-2.4 to 0.28)	-2.82 (-5.53 to -1.16)	-1.53 (-2.57 to -0.58)	-4.23 (-7.35 to -2.10)
<b>VF PSD (dB), median (IQR)</b>	1.74 (1.465 to 2.295)	3.08 (1.99 to 6.21)	1.72 (1.49 to 2.06)	3.74 (2.08 to 8.07)
<b>HRT rim area<sup>b</sup>, median (IQR)</b>	1.25 (1.09 to 1.53)	1.04 (0.83 to 1.29)	1.36 (1.19 to 1.61)	1.14 (0.91 to 1.42)
<b>CCT (μm), median (IQR)</b>	557 (531 to 580)	549 (524 to 573)	547 (528 to 563)	536 (513 to 557)
<b>Phacoemulsification in the past, n (%)</b>	7 (2)	65 (8)	2 (1)	74 (7)

CCT = central corneal thickness, HRT = Heidelberg retina tomography, IOP = intraocular pressure, NA = not acquired, OHT = ocular hypertension, POAG = primary open angle glaucoma, VF MD = visual field mean deviation, VF PSD = visual field pattern standard deviation

<sup>a</sup>The proportion of myopia was not reported in LiGHT UK

<sup>b</sup>Data were unavailable in 14 eyes with POAG and one eye with OHT, as severe cataract or high myopia

nificantly higher percentage of eyes were hyperopic in the POAG group and a significantly higher percentage of eyes were myopic in the OHT group (Chi-square test  $P = .002$ ). OHT and POAG eyes in the LiGHT China cohort were more myopic compared with the LiGHT UK cohort (OHT: median refractive error 0.44 D in LiGHT UK vs -1.5 D in LiGHT China; POAG: median refractive error 0.25 D in LiGHT UK vs -1.25 D in LiGHT China). Considering that the patients in the current cohort were significantly younger than the UK cohort, refractive diopter obtained from LiGHT China was further analyzed by different age groups. After adjusting for age, in patients > 50 years, the median of refractive error was 0.38 D in patients with OHT and -0.06 D with POAG (Table 5).

• **BASELINE DATA OF QUESTIONNAIRE SURVEY:** The detailed questionnaire survey results in LiGHT China are summarized in Table 6 and Table 7. There was no difference between patients with POAG and those with OHT on the GUI (difference -0.01, 95% CI -0.02 to 0.0004), VF-14 (dif-

ference 0.20, 95% CI -2.06 to 2.47) and GSS (difference -1.24, 95% CI -3.48 to 0.99); and the difference between OHT and POAG on the EQ-5D-5L in Chinese value version 0.024 (95% CI 0.01 to 0.04).

## DISCUSSION

The LiGHT China trial is aiming to compare eye drops versus SLT as the first-line treatment for newly diagnosed POAG or OHT patients. This is important, given the statistics that the prevalence of glaucoma in China fluctuated at around 2.6% from 1990 to 2015. In the future, the prevalence and burden of glaucoma will continue to increase with the current ageing trend in China.<sup>4</sup> According to statistics from the World Bank in 2018, the Gross Domestic Product (GDP) per capita (GDPPC) of China (\$9770.85) was less than 80 countries, including the USA (\$62641.01), the UK (\$42491.36) and Australia

**TABLE 5.** Refractive error in different age groups

Diagnosis	Variables		N (%)	Refractive error (Spherical D), median (IQR)
<b>OHT</b>	<b>Age group, years</b>	18-34	74 (49.7%)	-3.75 (-6.75 to 0.88)
		35-49	41 (27.5%)	-1.75 (-4.31 to -0.38)
		> 50	34 (22.8%)	0.38 (-0.88 to 0.78)
<b>POAG</b>	<b>Age group, years</b>	18-34	145 (23.3%)	-4.75 (-7.31 to -2.44)
		35-49	169 (27.2%)	-3.75 (-6.38 to -1.19)
		> 50	308 (49.5%)	-0.06 (-1.50 to 1.13)

OHT = ocular hypertension, POAG = primary open angle glaucoma

**TABLE 6.** Baseline value of questionnaires: LiGHT UK vs LiGHT China

	UK		China	
	OHT (n = 163)	POAG (n = 554)	OHT (n = 149)	POAG (n = 622)
<b>EuroQoL EQ-5D-5L Index, median (IQR)<sup>a</sup></b>	0.94 (0.89-1.00)	0.94 (0.88-1.00)	0.94 (0.89-0.94)	0.94 (0.86-1.00)
<b>Glaucoma Utility Index, median (IQR)</b>	0.93 (0.87-1.00)	0.90 (0.81-1.00)	0.96 (0.9-0.97)	0.96 (0.9-0.97)
<b>Glaucoma Symptom Scale, median (IQR)</b>	85 (75-95)	85 (73-95)	83 (75-91)	84 (74-90)
<b>Symptom, median (IQR)</b>	83 (71-100)	83 (71-96)	79 (67-88)	75 (63-88)
<b>Function, median (IQR)</b>	88 (75-100)	88 (75-100)	88 (81-100)	88 (85-100)
<b>Visual Function, median (IQR)</b>	NA	NA	84 (72-93)	86 (73-93)
<b>Glaucoma Quality of Life-15 (GQL-15)</b>	16 (15-19)	17 (15-21)	NA	NA

OHT = ocular hypertension, POAG = primary open angle glaucoma

<sup>a</sup>EQ-5D-5L Chinese version was used in LiGHT China and UK version in LiGHT UK

**TABLE 7.** Baseline value of questionnaires in LiGHT China: OHT vs POAG

	OHT (n = 149)	POAG (n = 622)	Difference (95% CI)
<b>EuroQoL EQ-5D-5L Index, Chinese value version, mean (SD)</b>	0.91 (0.08)	0.93 (0.07)	0.024 (0.01-0.04)
<b>Glaucoma Symptom Scale, mean (SD)</b>	82.07 (12.54)	80.83 (12.82)	-1.24 (-3.48-0.99)
<b>Glaucoma Utility Index, mean (SD)</b>	0.94 (0.06)	0.94 (0.06)	-0.01 (-0.02-0.0004)
<b>Visual Function-14, mean (SD)</b>	82.66 (12.38)	82.87 (13.03)	0.20 (-2.06-2.47)

OHT = ocular hypertension, POAG = primary open angle glaucoma

(\$57305.30). In 2016, China's expenditure on health was 5% of the GDP, which was lower than that of the USA (17.1%), the UK (9.8%) and Australia (9.3%). China still remains far behind developed countries in terms of GDP per capita and expenditure on health (percentage of GDP). Thus, from the perspective of a better cost-benefit ratio and quality of life of patients, there is a great need for China to evaluate treatment options for chronic eye diseases that require lifelong treatment, such as glaucoma.

Numerous studies to date have confirmed the beneficial effect of topical IOP-lowering medication in POAG and OHT patients, such as the European Glaucoma Prevention Study (EGPS),<sup>33</sup> the United Kingdom Glaucoma Treatment Study (UKGTS)<sup>34</sup> and the Ocular Hypertension Treatment Study (OHTS).<sup>35</sup> The LiGHT UK is the

first study to show that SLT, as the first-line treatment for POAG and OHT patients, is associated with definitive effectiveness, better health-related quality of life and lower cost compared with IOP-lowering drugs. However, there is a lack of RCT studies on the treatment of POAG and OHT in Asia, especially a lack of relevant literature on OHT, with most studies not reporting POAG and OHT separately. The LiGHT China trial is the first single-center randomized controlled trial conducted in Asia in association with LiGHT UK.

As shown in Table 1, the LiGHT China OHT and POAG cohorts were both significantly younger than in the LiGHT UK and other similar studies (OHTS: 55.4 years, UKGTS: 66 years) on average. The randomization process in LiGHT China achieved an appropriate equality of ages



for the two arms of the POAG and OHT cohorts. Therefore, it is still reliable to compare the primary outcome of two groups in the current study. The low age of the subjects is likely due to the fact that young people are more receptive to the "laser" and RCT trials, and more willing to participate in this study. Moreover, the lower age of the subjects in this study could be more relevant for the assessment of quality of life and cost of treatment because younger patients are associated with longer time needed to treat within life expectancy as well as higher costs of treatment. Additionally, their demands on quality of life may be different from those of slightly older patients.

Intraocular pressure (IOP) is currently the most commonly identified risk factor for glaucoma.<sup>36-39</sup> OHT eyes in the LiGHT China cohort had a mean IOP of 24.4 mm Hg, which was similar to that reported by OHTS (24.9 mm Hg) and EGPS (23.6 mm Hg), while the LiGHT China POAG cohort had overall lower IOPs than the LiGHT UK (mean IOP 21.0 mm Hg vs 23.5 mm Hg, respectively). In the current study, normal tension glaucoma (IOP < 21 mm Hg) accounted for 56% of the POAG patients, which was consistent with the epidemiological statistics in Asia<sup>40</sup> (range 46.9%-92.3%) and China (range 51.43%-83.58%).<sup>41</sup>

Eyes in the LiGHT China cohort were more myopic compared with LiGHT UK, which may be related to the lower age of the subjects. After grouping them according to age, it was found that the refraction error of patients > 50 years in the current study was still similar to other studies.<sup>42</sup>

In LiGHT China, the baseline mean visual field loss was more severe than in LiGHT UK and UKGTS (UKGTS: -2.90 dB), possibly indicating that only relatively severe glaucoma can get a patient's attention. A large number of patients come to the clinic only when they present with altered visual acuity and visual field loss. Severe glaucoma also necessitates patients' awareness of the need for life-long treatment, making them more willing to participate in the study. Considering the high refractive error of the subjects in LiGHT China and the relatively large proportion (21%) of high myopia (equivalent spherical lens > -6.00 D) in POAG patients, the higher glaucoma severity in the current study may also be associated with high myopia.

In the LiGHT China cohorts, 10% of OHT and 11% of POAG subjects reported a family history of glaucoma, which was significantly lower than that of LiGHT UK. Systemic hypertension was noted in 17.8% of the LiGHT China patients with POAG, which was lower than LiGHT UK and UKGTS (57.8%). Diabetes was recorded for 4.8% of the LiGHT China patients, which was lower than LiGHT UK and UKGTS (10.5%). Similarly, the prevalence of systemic hypertension and diabetes in the LiGHT China OHT cohort was significantly lower than that in the LiGHT UK OHT cohort and OHTS cohort (38% and 12%, respectively). As prevalence of hypertension and diabetes is age-related and economic development-related, the younger age of participants in LiGHT China explains the lower prevalence of the two diseases in this study. Additionally, no patients reported symptoms suggestive of vasospastic conditions in the LiGHT China cohort, while the prevalence of peripheral vasospastic symptoms was 14% for POAG and 4% for OHT in LiGHT UK. Five migraine sufferers were noted in the current study, while 13% of subjects in LiGHT UK reported a migraine history, possibly owing to the warmer climate and lower latitude in China.

Given differences in EQ-5D-5L value sets among countries<sup>31,32,43-45</sup> and the different specific preferences of general populations between China and UK, the EQ-5D-5L Chinese value set is recommended in LiGHT China to reflect the true societal preference in China. Mean EQ-5D-5L in LiGHT China was similar to that in LiGHT UK. As the interpretation and use of EQ-5D-5L response labels varies between non-English Asian countries and native English speaking countries,<sup>46</sup> care is needed when reporting results<sup>47</sup> and interpreting across cultures.

As shown in Table 6, mean GUI scores of POAG patients in LiGHT China were slightly higher than in LiGHT UK. Mean GSS of POAG patients in LiGHT China scored similar to LiGHT UK. One possible contributing factor could be the early stage of disease is most of the POAG in LiGHT China. The difference between OHT and POAG on the EQ-5D-5L in LiGHT China may be due to the culture and insufficient knowledge of POAG and OHT. There was no difference between POAG and OHT on EQ-5D-5L and GSS, GUI and VF-14. This might suggest that a better tool with which to discriminate between OHT and POAG in China is needed.

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