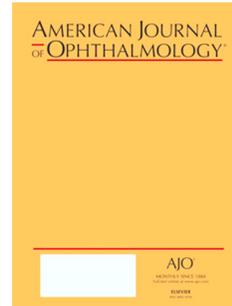


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Baseline characteristics of participants in the Treatment of Advanced Glaucoma Study (TAGS): A multicentre randomised controlled trial.

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Abstract

Purpose: To report the baseline characteristics of participants enrolled in the Treatment of Advanced Glaucoma Study (TAGS)

Design: Pragmatic randomised control trial (RCT).

Participants: Patients with open angle glaucoma presenting with advanced glaucoma in at least one eye as defined by the Hodapp-Parrish-Anderson (HPA) criteria of severe defect.

Methods Participants with newly diagnosed advanced glaucoma in at least one eye were recruited. Participants were randomly allocated to receive either primary augmented trabeculectomy or primary medical management. When both eyes were eligible, the same intervention was undertaken in both eyes and the index eye for analysis was the eye with the less severe visual field mean deviation (MD).

Main Outcome Measures: Visual field profile defined by the HPA classification, clinical characteristics, Quality of life measured by the National Eye Institute Visual Function Questionnaire 25 (VFQ-25), EuroQual-5 Dimension (EQ-5D 5L), Health Utility Index-3 (HUI-3) and Glaucoma Profile Instrument (GPI)

Results: Four hundred and fifty-three patients were recruited. The mean visual field MD was -15.0dB (SD 6.3) in the index eye and -6.2dB in the non-index eye. Of index eyes (HPA 'severe' classification) at baseline, over 70% had a mean deviation < -12.00dB and nearly 90% had more than 20 points defective at the 1% level. The mean LogMAR visual acuity of the index eye was 0.2 (SD 0.3),

Conclusions: TAGS is the first RCT to compare medical and surgical treatments for patients presenting with advanced open angle glaucoma in a publicly funded health service. It will provide clinical, health related quality of life and economic outcomes to inform future treatment choices for those presenting with advanced glaucoma

1 **Baseline characteristics of participants in the Treatment of Advanced Glaucoma Study (TAGS):**
2 **A multicentre randomised controlled trial.**

3

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33 **Key words**

34 Glaucoma, advanced glaucoma, glaucoma surgery, glaucoma drops, Quality of Life, Randomised

35 Clinical Trial.

36 **Abstract**

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55 index eye was 0.2 (SD 0.3),

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57 presenting with advanced open angle glaucoma in a publicly funded health service. It will
58 provide clinical, health related quality of life and economic outcomes to inform future
59 treatment choices for those presenting with advanced glaucoma

60 Introduction

61 Glaucoma is a common, chronic, irreversible, optic neuropathy affecting peripheral vision in
62 predominantly older adults(1) . Primary open angle glaucoma (POAG) affects over 2% of
63 those over 40 years(2). It is the second leading cause of blind registrations(3), a major cause
64 of disability in the elderly (4, 5) and worsening of Health-Related Quality of Life (HRQoL)(6-
65 11).

66

67 The incidence of POAG is estimated at 11,000 per year in people aged 40-70 in the UK(1, 12).
68 Approximately 1 in 4 patients present with advanced disease(13-17). However, the most
69 recent UK estimate (2006) indicated 39% of newly diagnosed cases had advanced disease in
70 at least one eye(18). Having advanced glaucoma at diagnosis is associated with a higher risk
71 of blindness compared with early stage detection(19-25).

72

73 Effective treatment stops or delays disease progression (26-28). The American Academy of
74 Ophthalmology does not specifically recommend a treatment approach for those presenting
75 with advanced glaucoma(29), however, in the UK, the National Institute of Health and Care
76 Excellence (NICE)(<https://www.nice.org.uk/guidance/ng81/chapter/Recommendations#treatment>)
77 recommends primary augmented trabeculectomy for patients presenting with advanced
78 glaucoma(1). A recent survey of ophthalmology consultants(30) suggests these guidelines are
79 not commonly adhered to within the UK because of concerns regarding surgery risk and
80 uncertainty about the best primary therapeutic option for such patients. The Treatment of
81 Advanced Glaucoma Study (TAGS) addresses this uncertainty and fulfils a recommendation of
82 a recent Cochrane review(31) to undertake research to determine whether primary medicine
83 or primary surgery is best for patients presenting with advanced glaucoma. TAGS will be the
84 first study to evaluate the best treatment for patients presenting with advanced glaucoma
85 who are those most at risk of developing blindness in their lifetime(19-23).

86

87 The primary objective of this report is to characterise the baseline features of the TAGS
88 cohort and further explore the profile of the advanced visual field loss in terms of the
89 Hodapp-Parrish-Anderson criteria of visual field loss.

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99 **Methods**

100 TAGS is a pragmatic multicentre randomised controlled trial and the design of the study has
101 been described in detail elsewhere(32). Eligible patients with advanced POAG in either eye
102 were randomised to have augmented trabeculectomy or IOP lowering drops as their primary
103 intervention and followed up for 24 months. Randomisation was based on the participant
104 (not the eye), but for those where both eyes were eligible, clinical outcomes are based on the
105 index eye defined as the eye with better mean deviation (MD) value.

106

107 *Disease Classification:* Eligible patients had primary open angle glaucoma (including pigment
108 dispersion and pseudoexfoliation). Advanced glaucoma was defined according to the
109 Hodapp-Parrish-Anderson (HPA) classification of severe glaucoma(33). At baseline
110 participants eligibility was determined with 2 SITA Standard 24-2 visual field examinations
111 and visual fields in addition to mean deviation value, were graded according to which of the 5
112 potential criteria defining severe glaucoma according to the HPA grading system they
113 fulfilled.

114

115 *Interventions:* In the primary medical treatment arm, participants start on one or more
116 medications (drops) at their initial visit depending upon the judgement of the treating
117 clinician and as advised by the NICE glaucoma guidelines(1) Subsequent additional
118 medication are based on clinician judgement. If drops fail to lower the IOP adequately, oral
119 carbonic anhydrase inhibitors may be used. If medical treatment fails patients will be offered
120 glaucoma surgery. In the primary trabeculectomy group, surgery should be undertaken
121 within three months of randomisation by a surgeon who specialises in glaucoma or a
122 glaucoma fellow who has performed at least 30 trabeculectomies. Patients IOP will be
123 medically controlled until glaucoma surgery is undertaken. Trabeculectomy will be
124 augmented with mitomycin-C. After glaucoma surgery, medical treatment may be introduced
125 if the IOP is above the desired target.

126 The dose of Mitomycin C in terms of exposure time and concentration was left to the
127 discretion of the operating surgeon and decided on a case by case basis. We believe this best
128 reflects what occurs in clinical practise. We acknowledge that different doses of MMC may
129 influence the IOP and adverse event outcomes associated with augmented trabeculectomy
130 surgery. However, the trial is designed to reflect real clinical practise and it is important to
131 measure these

132

133

134 *Inclusion/exclusion criteria:*

135 Included people who:

- 136 • had severe glaucomatous visual field loss (HPA classification) in one or both eyes at
137 presentation.

- 138 • had OAG including pigment dispersion glaucoma, pseudoexfoliative glaucoma and
139 normal tension glaucoma.
- 140 • were willing to participate in a trial.
- 141 • were able to provide informed consent.
- 142 • aged over 18 years.
- 143 • agreed, if female and of childbearing potential, to ensure that they used effective
144 contraception during the study and for three-months thereafter. A negative urine
145 pregnancy test for females of childbearing potential was required prior to
146 randomization.

147 Excluded people who

- 148 • were unable to undergo incisional surgery due to inability to lie flat or unsuitable for
149 anaesthetic.
- 150 • had a high-risk of trabeculectomy failure such as previous conjunctival surgery,
151 complicated cataract surgery.
- 152 • had secondary glaucomas, and primary angle-closure glaucoma.
- 153 • were pregnant, nursing, or planning a pregnancy or were females and of childbearing
154 potential not using a reliable method of contraception. A woman was considered to
155 be of childbearing potential unless she was without a uterus or was post-menopausal
156 and had been amenorrhic for at least 12 consecutive months.

157 Essentially everyone with advanced POAG (and who met the inclusion criteria) who could
158 have been treated with either one of the two treatment alternatives was invited to
159 participate in this study.

160

161 Outcome Measures: Clinical measurements for visual field loss MD and HPA Criteria on
162 Humphrey visual field testing. Logarithm of the mean angle of resolution (logMAR) visual
163 acuity (VA), intraocular pressure (IOP). Incidence of blindness(34) at diagnosis, family history
164 of glaucoma and self reported frequency of contact with primary care optometry in years
165 prior to diagnosis. Health Related Quality of Life (HRQoL) generic health status [EuroQual-5
166 dimension – 5 level (EQ-5D-5L)(35) and Health Utility Index (HUI-3)(36), visual health status
167 [National Eye Institute Visual Function Questionnaire 25 (VFQ-25)](37), glaucoma health
168 status [glaucoma utility index (GUI)](38), patient experience.

169

170 Follow-up: Patients will attend 4 scheduled study visits at baseline, 4, 12 and 24 months.
171 Clinical data is collected at each of these visits. HRQoL information is collected at baseline, 1,
172 3, 4, 6, 12, 18 and 24 months, and participant costs and healthcare utilisation for health
173 economic evaluation are collected at 4, 12, 18 and 24 months. The discrete choice
174 experiment was elicited at 27 months. Study schedule is described in Supplementary Table 1

175

176 *Statistical analysis:* Baseline characteristics are described using numbers and percentages for
177 dichotomous variables, numbers, median and interquartile range (IQR) for the number of
178 times the participant visited the optometrist in the last 10 years and mean and standard
179 deviation (SD) for all remaining continuous variables. For participants in whom both eyes
180 were eligible, data are summarised for both the index and non-index eye., In addition, for
181 visual fields MD, better eye (higher MD score) and worse eye (lower MD score) are also
182 reported. For participants who declined to participate in the trial, age and gender were
183 compared with participants randomised using a t-test and chi-squared test, respectively. EQ-
184 5D-5L was calculated following the method by Van Hout et al(39) and GUI was calculated
185 following the method by Burr et al(38) . All analyses were performed in Stata 15 software.
186 (40)
187
188
189

190 Results**191 Participant flow**

192 Eligible patients were recruited from 27 secondary care hospital centres in the UK between
193 3rd June 2014 and 31st May 2017 (Appendix 1). The trajectory of recruitment from all centres
194 is shown in Appendix 2.

195 There were 951 patients identified to be potentially eligible, of these 453 were randomised.
196 Patients (N=498) were excluded because they were ineligible (N=229) or declined (N=268);
197 for one participant the reason is unknown (Appendix 3). The commonest reason why patients
198 were not eligible was that they could not be randomised in the 3 months window following
199 diagnosis (23%) or the visual fields at screening visit did not fulfil eligibility criteria (23%). Of
200 those who declined to participate, the main reasons were they did not want to have surgery
201 (19%) or lifestyle considerations (16%); over 28% of patients did not indicate why they
202 declined. The reason why two patients were not randomised was not recorded (Appendix 3).

203 Baseline characteristics

204 The baseline participant characteristics are shown in Table 1. The mean age of participants
205 was 67 (SD 12.3) years, 303 (67%) of participants were male. For those individuals who
206 declined to participate in the trial (n=265), the mean age was slightly, but statistically
207 significantly, greater than that of participants at 69 (SD 12.8) years (p-value 0.04); 165 (62%)
208 were males (p-value 0.17). Participants were mainly Caucasian (82%)

209 Primary open angle glaucoma was the commonest form of open angle glaucoma accounting
210 for 97% of the cohort. Advanced glaucoma was present in both eyes in 19.4% of participants.

211 Baseline patient experience measures are shown in Table 2. The mean VFQ-25 was 87.1 (SD
212 13.5), the general vision and general health subscales were most affected. For generic health
213 status the HUI-3 scored lower than the EQ-5D-5L at 0.81 and 0.84 respectively and just over
214 one third (37.7%) self-reported that they felt their glaucoma was getting worse. There was a
215 10dB difference on average between the better eye visual field loss [-5.5 (SD 6.1) dB] and the
216 worse eye visual field loss [-15.7 (SD 6.7) dB] at presentation.

217 Baseline clinical characteristics for the index and non-index eye are shown in Table 3. The
218 eyes are similar for most measurements. However, the mean VF loss was greater in the
219 index eye (MD = -15.0 dB) compared to -6.2 dB in the non-index eye. Similarly, the IOP was
220 greater in the index eye both at diagnosis and baseline. The mean IOP at diagnosis and
221 baseline was 26.4 mmHg and 19.2 respectively and in the index eye and 22.9 and 17.9,
222 respectively, in the non-index eye. Participants were mainly taking prostaglandin analogue
223 drops at baseline, 81.2% in their index eye and 70.6% in their non-index eye. The mean visual
224 acuity was LogMAR 0.2 in the index eye and LogMAR 0.1 in the non-index eye. Binocular
225 visual acuity was LogMAR 0.1 (n =441; SD 0.01). Six percent of the cohort were eligible for
226 sight impairment registration in the UK at the time of diagnosis.

227 The vast majority of patients were phakic (>90%) and about a fifth had associated ocular co-
228 morbidity.

229 The HPA criteria leading to a 'severe' classification of glaucoma in the index eye at baseline is
230 shown in Table 4. Over 70% had a mean deviation < -12.00dB and nearly 90% for more than
231 20 points defective at the 1% level.

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239 **Discussion**

240 TAGS was designed to be a pragmatic trial comparing established options, medications or
241 surgery, as initial treatment for people diagnosed with severe glaucoma. Only the primary
242 intervention was dictated by the trial protocol (32).

243 The term “pragmatic” for RCTs was introduced half a century ago(41). In contrast to “
244 explanatory” RCTs that test hypotheses on whether the intervention causes an outcome of
245 interest in ideal circumstances, “pragmatic” RCTs aim to provide information on the
246 relative merits of real-world clinical alternatives in routine care. A pragmatic RCT focuses on
247 maximizing external validity (generalizability of the results to many real-world settings).
248 Pragmatic RCTs help to inform decisions by clinicians, patients and policy makers. In a
249 challenging health-cost environment, Health Technology Assessment agencies and Managed
250 Care Organizations want to have real-world evidence on comparative effectiveness of
251 available interventions in clinical practice to inform their decisions. A genuinely pragmatic
252 RCT should fulfil at least two fundamental features. First, its conduct should resemble usual
253 clinical practice. Second, the results should be applicable to multiple other settings, not only
254 the one where the trial was conducted. Consequently, in principle, pragmatic RCTs should
255 assess already available interventions and should be done in several sites providing care to
256 heterogeneous populations(42).

257 Recruitment to RCTs comparing surgical and non-surgical interventions can be
258 challenging(43). TAGS recruited to time and to target which may reflect the considerable pre-
259 trial effort to ensure that the trial was conducted in a way acceptable to patients and
260 information presented in a way that was understood(44).

261 Nearly one third of our cohort reported a family history of glaucoma which is similar to three
262 previous primary intervention studies of patients with early glaucoma(45-47). Suggesting that
263 having a family history of glaucoma does not reduce your risk of presenting with advanced
264 disease.

265 One mechanism for minimising risk of presentation with advanced glaucoma is a regular visit
266 to an eye care professional. In England, current policy facilitates visits to a community
267 optometrist annually for those over 40 years with a family history of glaucoma. In addition,
268 all people over the age of 60 years are entitled to a free eye test every 2 years. Nearly one
269 third of the participants in TAGS had a known family history of glaucoma (so entitled to
270 annual glaucoma screening) and the vast majority were over 60 years old. The participants
271 report a median of 5 visits to their optometrist in the 10 years prior to diagnosis with
272 advanced glaucoma. These findings suggest that, despite a robust public health provision to
273 prevent diagnosis with advanced disease, a large number of patients are still not being
274 diagnosed at an early stage. Indeed over 6% of the cohort were eligible for sight impairment
275 registration in the UK at the time of diagnosis(34). The reason these opportunities to
276 diagnose glaucoma earlier are missed is unknown. It is possible that participants have some

277 recall bias and over-estimated the frequency of visits to their optometrists prior to diagnosis
278 or that they were rapid progressors as previously suggested by Fraser(48). However, it has
279 also been suggested that delays in diagnosis may occur at several points, from failure of
280 recognition/diagnosis of glaucoma by optometrists, to failure to refer appropriately or delays
281 in this process occurring(49).

282 One reason this reduced vision may not have prompted patients to seek attention earlier is a
283 resignation among older people that poorer vision is a natural consequence of ageing(50)
284 and they may not therefore pay much attention to the subtle and slowly developing
285 deterioration associated with visual field loss, especially if only affecting one eye .

286 Visual Field loss

287 VF damage is the major clinical measure of the functional impact of glaucoma, which
288 adversely influences QoL(8, 9, 51, 52).

289
290 There are few RCTS which have explored treatment outcomes in patients with advanced
291 glaucoma and none which have explored primary interventions in a treatment naïve cohort.
292 In the TAGS, the mean visual field MD score of the index eye was -15.0 dB. Although an
293 Advanced Glaucoma Intervention Study (AGIS) has already been undertaken, that study
294 defined 'advanced' as "When maximum effective, accepted, and tolerated medications fail to
295 reduce intraocular pressure adequately and there has been some visual field loss, the patient
296 is said to have advanced glaucoma"(53). In AGIS the extent of visual field loss was not an
297 entry criterion. The MD for the AGIS cohort was not reported as a whole but was about -
298 10.5 dB (mean defect -11.3dB for black participants and -9.4dB for white participants(54).
299 In AGIS, participants had also already exhausted possible medical interventions. The Tube
300 Versus Trab (TVT) study recruited participants with previous surgical intervention and an MD
301 of -16.7 (SD 9.32) dB, however the patients had uncontrolled glaucoma already, despite
302 previous medical and surgical interventions(55). Similarly, the Primary Tube Versus Trab
303 study (PTVT) recruited patients with inadequately controlled glaucoma on maximum
304 tolerated medical therapy but no previous surgery; these patients had an MD of -14.7 dB(56).
305 Neither of these study cohorts examines primary interventions in treatment naïve patients
306 with advanced glaucoma and all tested different interventions compared to those being
307 explored by TAGS.

308 There have been several previous RCTs of primary medical versus surgical treatment(31). In
309 these, disease severity has been variable, and, since they were undertaken, medical and
310 surgical interventions have evolved. In the Moorfields Glaucoma Trial, the stage of glaucoma
311 was not described(57, 58). In the Glasgow Trial, 35% of participants had severe glaucoma
312 (according to the study definition)(59). In the Moorfields Primary Treatment Trial, 48% of
313 participants had severe glaucoma (according to the study definition >12 absolute defects on
314 Friedman perimetry)(60). In CIGTS, most participants had mild glaucoma based on the
315 average MD of -5.5 dB; one hundred and sixty-eight (27%) participants had no visual field

316 defect, and were included on the basis of IOP \geq 27 mmHg and an optic disc appearance
317 compatible with glaucoma. Thus, TAGS is the first and largest cohort of patients with
318 advanced glaucoma evaluated with the Humphrey Visual Field Analyser which will provide a
319 more precise method of evaluation of long-term visual field changes in patients with primary
320 advanced visual field loss.

321

322 Two recent RCTs assessing treatment in OAG, the Laser in Glaucoma and Ocular
323 Hypertension Trial (LiGHT)(28) and the United Kingdom Glaucoma Treatment Study
324 (UKGTS)(27) recruited cohorts with mild glaucoma. In the LiGHT, the mean baseline MD for
325 the OHT participants was -1.25 (SD 2.05) dB and for POAG participants was -3.81 (SD 3.68) dB
326 and for UKGTS the median (IQR) baseline VF loss was -2.9 (-1.6 - -4.8) dB so both these
327 cohorts had considerably less baseline VF loss than those entered into TAGS. TAGS,
328 therefore, provides valuable information not already available for patients presenting with
329 advanced visual field loss and complements previously undertaken studies exploring
330 interventions in patients with mild visual field loss.

331

332 Quality of Life

333 Glaucoma is a bilateral disease and the severity of visual field loss in both the more and less
334 affected eyes affects the VFQ-25 score(10, 61). Additionally, central location of visual
335 field(62) loss also decreases HRQoL. For patients with progressive glaucoma, having more
336 advanced binocular loss disproportionately results in more HRQoL reduction for each further
337 dB loss of visual field(11). Table 4 demonstrates that both global and localised central
338 defects are well represented in the cohort ensuring that TAGS is uniquely designed to explore
339 further these observations in a large group of patients with advanced glaucoma.

340

341 No previous primary treatment RCTs for advanced glaucoma have assessed patients reported
342 outcomes. The Tube versus Trabeculectomy (TVT) study reported the VFQ-25 in patients
343 with advanced glaucoma but these patients had longstanding glaucoma prior to
344 recruitment(63). For the TAGS, the vision specific VFQ-25 composite score was 87.1 (SD
345 13.5) which is better than the level reported in the TVT study of 71.9 (SD 17.9). This
346 difference may reflect that patients in the TVT study had longstanding glaucoma, had
347 previous incisional surgery prior to recruitment and a mean visual field MD of -16.7dB. As the
348 VFQ-25 is a measurement influenced by bilateral visual function(10, 61), rather than just the
349 index eye visual function, it is possible that patients in TVT with longstanding glaucoma also
350 had worse baseline visual function in the non-index eye.

351

352 TAGS is the first study of patients with advanced glaucoma to report values for the generic
353 health status instrument EQ-5D-5L. One previous study of patients with early POAG and OHT
354 (LiGHT), reported an average value of 0.92 (SD 0.13), which is better than that recorded for
355 TAGS of 0.84 (0.18) suggesting a considerable difference in generic HRQoL for patients with
356 advanced glaucoma compared to those with early disease, albeit that the LiGHT cohort were

357 on average about 3 years younger (64.1 vs 67.2) than TAGS patients at baseline. To explore
358 whether including a generic health instrument with a vision specific domain better reflects
359 HRQoL in patients with advanced glaucoma, we also collected data with the HUI-3, which
360 found a small 3 point score reduction compared with the EQ-5D-5L. It is, therefore, uncertain
361 if the HUI-3 incorporating vision disability into its composite score is more effective as a
362 generic HRQoL in patients whose vision is affected. Long term follow-up of the TAGS cohort
363 will provide further insight into which, if any, of these two measurement tools is more
364 effective in capturing change in glaucoma status.

365
366 The GUI was used to report glaucoma specific health status. For the GUI in LiGHT, the mean
367 score was 0.89 for the POAG group(47). In TAGS the mean score was also 0.89 (SD 0.12). This
368 suggests a poor ability for the GUI to discriminate between early and late disease, and this
369 may reflect the modest number of people in the reference cohort of GUI development with
370 advanced glaucoma(38). However, this may alternatively be a reflection that there was
371 relatively good function of the non-index eye in many of our cohort, masking this difference.

372
373 Although several previous RCTs of primary medication vs trabeculectomy have been
374 undertaken only one collected any patient-reported outcome measures (PROMS)(64, 65).
375 The Collaborative Initial Glaucoma Treatment Study (CIGTS) recruited patients with early
376 glaucoma and collected a battery of PROMS reporting both systemic and local effects of
377 treatment. There was no difference at baseline between surgery and medicine groups in this
378 study(65), however it did not use any of the instruments employed in the TAGS. TAGS is the
379 first study where generic, vision and glaucoma specific PROMS have been collected
380 systematically in patients with advanced disease at presentation and the first glaucoma RCT
381 to report HUI-3, which contains a vision specific domain.

382
383 In conclusion, the baseline characteristics of the TAGS cohort show advanced visual field loss
384 is well represented with both global and central visual field loss at baseline. This cohort
385 provides a unique opportunity to establish which primary interventions best preserves the
386 vision of those presenting with advanced glaucoma

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395 **Trial Registration Number:** ISRCTN56878850,

396 **Disclaimer:** The views expressed are those of the authors and not necessarily those of the
397 NHS, the NIHR or the Department of Health.

398 **Ethics approval:** The study adheres to the tenets of the Declaration of Helsinki and the
399 principles of Good Clinical Practice (GCP), and is in accordance with all applicable regulatory
400 guidance, including, but not limited to, the Research Governance Framework. TAGS' protocol
401 and patient-facing documentation were prospectively reviewed and approved by the Derby 1
402 Research Ethics Committee (ref number 13/EM/00395). Local NHS Research and
403 Development (R&D) approvals were obtained prior to commencement of the trial at the
404 participating sites. An independent data and safety monitoring committee oversees

405

406 **References**

- 407 1. Glaucoma: diagnosis and mangement. NICE CG85. London: National Institute for Health and
408 Care Excellence; 2009. Available from: <https://www.nice.org.uk/guidance/cg85>.
- 409 2. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020.
410 *Br J Ophthalmol*. 2006;90(3):262-7.
- 411 3. Bunce C, Xing W, Wormald R. Causes of blind and partial sight certifications in England and
412 Wales: April 2007-March 2008. *Eye (Lond)*. 2010;24(11):1692-9.
- 413 4. Haymes SA, Leblanc RP, Nicolela MT, Chiasson LA, Chauhan BC. Risk of falls and motor
414 vehicle collisions in glaucoma. *Invest Ophthalmol Vis Sci*. 2007;48(3):1149-55.
- 415 5. Haymes SA, LeBlanc RP, Nicolela MT, Chiasson LA, Chauhan BC. Glaucoma and on-road
416 driving performance. *Invest Ophthalmol Vis Sci*. 2008;49(7):3035-41.
- 417 6. Parrish RK, 2nd, Gedde SJ, Scott IU, Feuer WJ, Schiffman JC, Mangione CM, et al. Visual
418 function and quality of life among patients with glaucoma. *Arch Ophthalmol*. 1997;115(11):1447-55.
- 419 7. Nelson P, Aspinall P, O'Brien C. Patients' perception of visual impairment in glaucoma: a pilot
420 study. *Br J Ophthalmol*. 1999;83(5):546-52.
- 421 8. Nelson P, Aspinall P, Papisouliotis O, Worton B, O'Brien C. Quality of life in glaucoma and its
422 relationship with visual function. *J Glaucoma*. 2003;12(2):139-50.
- 423 9. Gutierrez P, Wilson MR, Johnson C, Gordon M, Cioffi GA, Ritch R, et al. Influence of
424 glaucomatous visual field loss on health-related quality of life. *Arch Ophthalmol*. 1997;115(6):777-
425 84.
- 426 10. McKean-Cowdin R, Wang Y, Wu J, Azen SP, Varma R, Los Angeles Latino Eye Study G. Impact
427 of visual field loss on health-related quality of life in glaucoma: the Los Angeles Latino Eye Study.
428 *Ophthalmology*. 2008;115(6):941-8 e1.
- 429 11. Medeiros FA, Gracitelli CP, Boer ER, Weinreb RN, Zangwill LM, Rosen PN. Longitudinal
430 changes in quality of life and rates of progressive visual field loss in glaucoma patients.
431 *Ophthalmology*. 2015;122(2):293-301.
- 432 12. Burr JM, Mowatt G, Hernandez R, Siddiqui MA, Cook J, Lourenco T, et al. The clinical
433 effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and
434 economic evaluation. *Health Technol Assess*. 2007;11(41):iii-iv, ix-x, 1-190.
- 435 13. Coffey M, Reidy A, Wormald R, Xian WX, Wright L, Courtney P. Prevalence of glaucoma in the
436 west of Ireland. *Br J Ophthalmol*. 1993;77(1):17-21.
- 437 14. Sheldrick JH, Ng C, Austin DJ, Rosenthal AR. An analysis of referral routes and diagnostic
438 accuracy in cases of suspected glaucoma. *Ophthalmic Epidemiol*. 1994;1(1):31-9.
- 439 15. Elkington AR, MacKean J, P. S. A collaborative hospital glaucoma survey. *Res Clin Forums*.
440 1982;4:31-40.
- 441 16. Boodhna T, Crabb DP. Disease severity in newly diagnosed glaucoma patients with visual
442 field loss: trends from more than a decade of data. *Ophthalmic Physiol Opt*. 2015;35(2):225-30.
- 443 17. Sukumar S, Spencer F, Fenerty C, Harper R, Henson D. The influence of socioeconomic and
444 clinical factors upon the presenting visual field status of patients with glaucoma. *Eye*.
445 2009;23(5):1038-44.
- 446 18. Ng WS, Agarwal PK, Sidiki S, McKay L, Townend J, Azuara-Blanco A. The effect of socio-
447 economic deprivation on severity of glaucoma at presentation. *British Journal of Ophthalmology*.
448 2010;94(1):85-7.
- 449 19. Peters D, Bengtsson B, Heijl A. Factors associated with lifetime risk of open-angle glaucoma
450 blindness. *Acta Ophthalmol*. 2014;92(5):421-5.
- 451 20. Grant WM, Burke JF, Jr. Why do some people go blind from glaucoma? *Ophthalmology*.
452 1982;89(9):991-8.
- 453 21. Mokhles P, Schouten JS, Beckers HJ, Azuara-Blanco A, Tuulonen A, Webers CA. A Systematic
454 Review of End-of-Life Visual Impairment in Open-Angle Glaucoma: An Epidemiological Autopsy. *J*
455 *Glaucoma*. 2016;25(7):623-8.

- 456 22. Odberg T. Visual field prognosis in advanced glaucoma. *Acta Ophthalmol* 1987;65 (suppl):27-
457 9.
- 458 23. Oliver JE, Hattenhauer MG, Herman D, Hodge DO, Kennedy R, Fang-Yen M, et al. Blindness
459 and glaucoma: a comparison of patients progressing to blindness from glaucoma with patients
460 maintaining vision. *Am J Ophthalmol*. 2002;133(6):764-72.
- 461 24. Mikelberg FS, Schulzer M, Drance SM, Lau W. The rate of progression of scotomas in
462 glaucoma. *Am J Ophthalmol*. 1986;101(1):1-6.
- 463 25. Wilson R, Walker AM, Dueker DK, Crick RP. Risk factors for rate of progression of
464 glaucomatous visual field loss: a computer-based analysis. *Arch Ophthalmol*. 1982;100(5):737-41.
- 465 26. Maier PC, Funk J, Schwarzer G, Antes G, Falck-Ytter YT. Treatment of ocular hypertension
466 and open angle glaucoma: meta-analysis of randomised controlled trials. *BMJ*. 2005;331(7509):134.
- 467 27. Garway-Heath DF, Crabb DP, Bunce C, Lascaratos G, Amalfitano F, Anand N, et al.
468 Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial.
469 *Lancet*. 2015;385(9975):1295-304.
- 470 28. Gazzard G, Konstantakopoulou E, Garway-Heath D, Garg A, Vickerstaff V, Hunter R, et al.
471 Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and
472 glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet*. 2019;393(10180):1505-16.
- 473 29. American Academy of Ophthalmology. Primary Open Angle Glaucoma: Preferred Practise
474 Patterns. Elsevier Inc; 2105.
- 475 30. Stead R, Azuara-Blanco A, King AJ. Attitudes of consultant ophthalmologists in the UK to
476 initial management of glaucoma patients presenting with severe visual field loss: a national survey.
477 *Clin Experiment Ophthalmol*. 2011;39(9):858-64.
- 478 31. Burr J, Azuara-Blanco A, Avenell A, Tuulonen A. Medical versus surgical interventions for
479 open angle glaucoma. *Cochrane Database of Systematic Reviews*. 2012:DOI:
480 10.1002/14651858.CD004399.pub3.
- 481 32. King AJ, Fernie G, Azuara-Blanco A, Burr JM, Garway-Heath T, Sparrow JM, et al. Treatment
482 of Advanced Glaucoma Study: a multicentre randomised controlled trial comparing primary medical
483 treatment with primary trabeculectomy for people with newly diagnosed advanced glaucoma-study
484 protocol. *Br J Ophthalmol*. 2017.
- 485 33. Hodapp E, Parrish RK, Anderson DR. Clinical decision in glaucoma. St Louis MO: Mosby;
486 1993.
- 487 34. Department of Health. Certificate of Vision Impairment: Explanatory Notes for Consultant
488 Ophthalmologists and Hospital Eye Clinic Staff in England. Leeds: Department of Health; 2017
489 [Available from:
490 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/637590/CVI_guidance.pdf.
491 /637590/CVI_guidance.pdf.
- 492 35. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and
493 preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*.
494 2011;20(10):1727-36.
- 495 36. Tosh J, Brazier J, Evans P, Longworth L. A review of generic preference-based measures of
496 health-related quality of life in visual disorders. *Value Health*. 2012;15(1):118-27.
- 497 37. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD, et al. Development of the
498 25-item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol*. 2001;119(7):1050-8.
- 499 38. Burr JM, Kilonzo M, Vale L, Ryan M. Developing a preference-based Glaucoma Utility Index
500 using a discrete choice experiment. *Optom Vis Sci*. 2007;84(8):797-808.
- 501 39. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, et al. Interim scoring
502 for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health*. 2012;15(5):708-15.
- 503 40. StataCorp. Stata Statistical Software: Release 15. College Station, TX:: StataCorp LLC; 2017.
- 504 41. Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. *J Chronic*
505 *Dis*. 1967;20(8):637-48.

- 506 42. Dal-Re R, Janiaud P, Ioannidis JPA. Real-world evidence: How pragmatic are randomized
507 controlled trials labeled as pragmatic? *BMC Med.* 2018;16(1):49.
- 508 43. Cook JA, Ramsay CR, Norrie J. Recruitment to publicly funded trials--are surgical trials really
509 different? *Contemp Clin Trials.* 2008;29(5):631-4.
- 510 44. Leighton P, Lonsdale AJ, Tildsley J, King AJ. The willingness of patients presenting with
511 advanced glaucoma to participate in a trial comparing primary medical vs primary surgical
512 treatment. *Eye (Lond).* 2012;26(2):300-6.
- 513 45. Lascaratos G, Garway-Heath DF, Burton R, Bunce C, Xing W, Crabb DP, et al. The United
514 Kingdom Glaucoma Treatment Study: a multicenter, randomized, double-masked, placebo-
515 controlled trial: baseline characteristics. *Ophthalmology.* 2013;120(12):2540-5.
- 516 46. Musch DC, Lichter PR, Guire KE, Standardi CL. The Collaborative Initial Glaucoma Treatment
517 Study: study design, methods, and baseline characteristics of enrolled patients. *Ophthalmology.*
518 1999;106(4):653-62.
- 519 47. Konstantakopoulou E, Gazzard G, Vickerstaff V, Jiang Y, Nathwani N, Hunter R, et al. The
520 Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre randomised controlled trial:
521 baseline patient characteristics. *Br J Ophthalmol.* 2018;102(5):599-603.
- 522 48. Fraser S, Bunce C, Wormald R. Risk factors for late presentation in chronic glaucoma. *Invest*
523 *Ophthalmol Vis Sci.* 1999;40(10):2251-7.
- 524 49. Prior M, Francis JJ, Azuara-Blanco A, Anand N, Burr JM, Glaucoma screening Platform Study
525 g. Why do people present late with advanced glaucoma? A qualitative interview study. *Br J*
526 *Ophthalmol.* 2013;97(12):1574-8.
- 527 50. Patel D BH, Murdoch I. Barriers to uptake of eye careservices by the Indian population living
528 in Ealing, WestLondon. . *Health Educ J* 2006;65(3):267-76.
- 529 51. Hyman LG, Komaroff E, Heijl A, Bengtsson B, Leske MC, Early Manifest Glaucoma Trial G.
530 Treatment and vision-related quality of life in the early manifest glaucoma trial. *Ophthalmology.*
531 2005;112(9):1505-13.
- 532 52. Jampel HD, Friedman DS, Quigley H, Miller R. Correlation of the binocular visual field with
533 patient assessment of vision. *Invest Ophthalmol Vis Sci.* 2002;43(4):1059-67.
- 534 53. Ederer F, Gaasterland DE, Sullivan EK, Investigators A. The Advanced Glaucoma Intervention
535 Study (AGIS): 1. Study design and methods and baseline characteristics of study patients. *Control Clin*
536 *Trials.* 1994;15(4):299-325.
- 537 54. The Advanced Glaucoma Intervention Study (AGIS): 3. Baseline characteristics of black and
538 white patients. *Ophthalmology.* 1998;105(7):1137-45.
- 539 55. Gedde SJ, Schiffman JC, Feuer WJ, Parrish RK, 2nd, Heuer DK, Brandt JD, et al. The tube
540 versus trabeculectomy study: design and baseline characteristics of study patients. *Am J*
541 *Ophthalmol.* 2005;140(2):275-87.
- 542 56. Gedde SJ, Chen PP, Heuer DK, Singh K, Wright MM, Feuer WJ, et al. The Primary Tube Versus
543 Trabeculectomy Study: Methodology of a Multicenter Randomized Clinical Trial Comparing Tube
544 Shunt Surgery and Trabeculectomy with Mitomycin C. *Ophthalmology.* 2018;125(5):774-81.
- 545 57. Smith R. A comparison between medical and surgical treatment of glaucoma simplex--results
546 of a prospective study. *Transactions of the Ophthalmological Society of Australia.* 1968;27:17-29.
- 547 58. Smith R. A current study of the Moorfields glaucoma trial. *Trans Ophthalmol Soc U K.*
548 1970;90:861-8.
- 549 59. Jay JL, Murray SB. Early trabeculectomy versus conventional management in primary open
550 angle glaucoma. *Br J Ophthalmol.* 1988;72(12):881-9.
- 551 60. Migdal C, Gregory W, Hitchings R, Kolker AE. Long-term functional outcome after early
552 surgery compared with laser and medicine in open-angle glaucoma. *Ophthalmology.*
553 1994;101(10):1651-7.
- 554 61. McKean-Cowdin R, Varma R, Wu J, Hays RD, Azen SP, Los Angeles Latino Eye Study G.
555 Severity of visual field loss and health-related quality of life. *Am J Ophthalmol.* 2007;143(6):1013-23.

- 556 62. Abe RY, Diniz-Filho A, Costa VP, Gracitelli CP, Baig S, Medeiros FA. The Impact of Location of
557 Progressive Visual Field Loss on Longitudinal Changes in Quality of Life of Patients with Glaucoma.
558 Ophthalmology. 2016;123(3):552-7.
- 559 63. Kotecha A, Feuer WJ, Barton K, Gedde SJ, Tube Versus Trabeculectomy Study G. Quality of
560 Life in the Tube Versus Trabeculectomy Study. Am J Ophthalmol. 2017;176:228-35.
- 561 64. Janz NK, Wren PA, Lichter PR, Musch DC, Gillespie BW, Guire KE. Quality of life in newly
562 diagnosed glaucoma patients : The Collaborative Initial Glaucoma Treatment Study. Ophthalmology.
563 2001;108(5):887-97; discussion 98.
- 564 65. Janz NK, Wren PA, Lichter PR, Musch DC, Gillespie BW, Guire KE, et al. The Collaborative
565 Initial Glaucoma Treatment Study: interim quality of life findings after initial medical or surgical
566 treatment of glaucoma. Ophthalmology. 2001;108(11):1954-65.

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Table 1 Baseline demographic and clinical characteristics for participants in the Treatment of Advanced Glaucoma Study (TAGS)

	N=453	
	n	%
Age (years) - n; mean (SD)	453	67.2 (12.3)
Gender		
Male	303	66.9
Female	150	33.1
Ethnicity		
Caucasian	373	82.3
Afro-Caribbean	59	13.0
Asian - India/Pakistan/Bangladesh	12	2.6
Asian - Oriental	2	0.4
Mixed heritage	1	0.2
Other	5	1.1
Missing	1	0.2
Advanced glaucoma in both eyes		
Yes	88	19.4
No	365	80.6
Glaucoma in both eyes		
Yes	347	76.6
No	106	23.4
Eligible to be registered as sight impaired		
No	426	94.0
Sight impaired	22	4.9
Severe sight impaired	5	1.1
Glaucoma diagnosis		
Primary open angle glaucoma (including NTG)	439	96.9
Pigment dispersion syndrome	9	2.0
Psuedoexfoliation syndrome	5	1.1
Family history of glaucoma		
Yes	142	31.3
No	283	62.5
Missing	28	6.2
Number of times visited the optician in the last 10 year – n; median [IQR]	423	5 [3, 7]
Visual fields mean deviation (dB) for the better eye - n; mean (SD)	451	-5.5 (6.1)
Visual fields mean deviation for the worst eye (dB) - n; mean (SD)	453	-15.7 (6.7)

Table 2 - Baseline participants' "patient reported outcomes" in the Treatment of Advanced Glaucoma Study (TAGS)

	N=453	
	n	n (SD)
NEI-VFQ-25	450	87.1 (13.5)
NEI-VFQ-25 subscales		
Near activities	449	84.3 (17.7)
Distance activities	450	89.1 (15.3)
Dependency	448	94.5 (16.5)
Driving	329	85.4 (26.4)
General health	448	62.2 (23.0)
Role difficulties	448	87.2 (20.2)
Mental health	450	81.4 (20.5)
General vision	446	73.9 (14.3)
Social function	449	95.1 (12.0)
Colour vision	445	96.7 (11.0)
Peripheral vision	448	86.9 (20.5)
Ocular pain	449	84.3 (18.1)
EQ-5D-5L - n; mean (SD)	444	0.840 (0.180)
EQ-5D-VAS - n; mean (SD)	445	82.2 (15.8)
HUI-3 - n; mean (SD)	428	0.812 (0.205)
GUI - n; mean (SD)	441	0.891 (0.123)
Participant experience (glaucoma getting worse) - n (%)		
Yes	171	37.7
No	246	54.3
Missing	36	7.9

SD standard deviation; NEI-VFQ-25 – National Eye Institute Visual Function Questionnaire-25; EQ-5D-5L – EuroQual 5 Dimension 5 Level; EQ-5D-VAS – EuroQual 5 Dimension Visual Analogue Scale; HUI-3 Health Utility Index-3; GUI – Glaucoma Utility Index

Table 3 – Baseline clinical characteristics for index and non-index eye of participants in the Treatment of Advanced Glaucoma Study (TAGS)

	Index eye N=453 n (%)	Non-index eye N=453 n (%)
Lens status		
Phakic	421 (92.9)	418 (92.3)
Psuedophakic	32 (7.1)	34 (7.5)
Missing	-	1 (0.2)
Central corneal thickness (μm) - n; mean (SD)	449; 540.4 (35.6)	448; 540.9 (36.8)
Drops	453; 1, [1, 2]	453; 1, [0, 1]
PG analogue	368 (81.2)	320 (70.6)
β -blocker	104 (23.0)	82 (18.1)
CA inhibitor	78 (17.2)	54 (11.9)
Agonist	11 (2.4)	7 (1.6)
Diamox ¹	8 (1.8)	-
Ocular co-morbidity		
Yes	100 (22.1)	98 (21.6)
No	353 (77.9)	355 (78.4)
Ocular co-morbidity details ²		
AMD	10 (10.0)	10 (10.2)
Cataract	84 (84.0)	79 (80.6)
Vascular occlusion	3 (3.0)	2 (2.0)
Diabetic retinopathy	2 (2.0)	2 (2.0)
other	15 (15.0)	22 (22.4)
Visual fields mean deviation (dB) - n; mean (SD)	453; -15.1 (6.3)	451; -6.1 (7.4)
LogMAR visual acuity - n; mean (SD)	450; 0.2 (0.3)	448; 0.1 (0.2)
Intraocular pressure (mmHg) - n; mean (SD)		
Diagnosis	449; 26.4 (8.8)	448; 22.9 (7.0)
Baseline	443; 19.2 (5.9)	442; 17.9 (4.7)

¹taken orally. ²participants can have more than one, PG – prostaglandin; CA – carbonic anhydrase

Table 4 – Hodapp-Parrish-Anderson criteria for ‘severe’ glaucoma (index eye) at baseline for participants in the Treatment of Advanced Glaucoma Study (TAGS)

	Visual Fields N=453	
	n	%
Mean deviation < -12.00dB	324	71.5
More than 20 points defective at the 1% level	405	89.4
A point in the central 5 degrees has a sensitivity of 0-dB	272	60.0
More than 50% of points defective in the pattern deviation probability plot at the 5% level	395	87.2
Points with 5 degrees of fixation under 15 dB sensitivity in both upper and lower hemi-fields	93	20.5