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Precis

For patients presenting with advanced glaucoma SES influences disease severity at presentation but has no effect on success of either medical or surgical treatment interventions.

Key Messages

What is already known on this topic

Poorer SES is known to increase the risk of presenting with advanced glaucoma.

What this study adds

This study demonstrates that those presenting with already advanced glaucoma are from poorer SES background and have worse visual field loss in both eyes and poorer vision related QoL, however SES does not affect the success of treatment.

How this study may affect research, practice or policy

This study further emphasises the need to increase awareness of glaucoma and improve health seeking behaviour amongst those from poorer SES.

Abstract

Background/Aims: Socio-economic status (SES) is associated with late disease presentation and poorer outcomes. We evaluate the effect of SES on treatment outcomes and report the correlation between SES and baseline characteristics of participants in the Treatment of Advanced Glaucoma Study.

Methods: Pragmatic multicentre randomised control trial. Four hundred and fifty-three patients presenting with advanced open angle glaucoma in at least one eye [Hodapp-Parrish-Anderson classification]. Participants were randomised to either glaucoma drops (medical arm) or trabeculectomy (surgery arm). Clinical characteristics, Quality of life measurement (QoL) and SES defined by the index of multiple deprivation (IMD) are reported. Subgroup analysis explored treatment effect modifications of SES at 24 months. Correlation between SES and baseline characteristics was tested with the Chi-squared test of association for dichotomous variables and Pairwise Pearson's correlation for continuous variables.

Results: The mean visual field MD was -17.2(6.7)dB for the most deprived quintile of participants and -13.0(5.5) for the least deprived quintile in the index eye. At diagnosis there was a strong correlation between SES and ethnicity, age, extent of visual field loss and number of visits to opticians prior to diagnosis. At 24 months there was no evidence that the treatment effect was moderated by SES.

Conclusions: In patients presenting with advanced glaucoma,. SES at baseline is correlated with poorer visual function, poorer VFQ-25 quality of life, ethnicity, age and number visits to an optician in the years preceding diagnosis. SES at baseline does not have an effect of the success of treatment at 24 months

Trial registration: Health Technology Assessment (NIHR-HTA) Programme (Project number: 12/35/38). ISRCTN registry: ISRCTN56878850

Introduction

Socioeconomic inequality is recognised to contribute to poorer health outcomes for those from poorer socioeconomic backgrounds in the UK (1) and North America (2-4).

Glaucoma is a chronic progressive eye disease, with substantial and detrimental effects on numerous aspects of daily living(5) a major cause of disability in the elderly (6,7) and worsening of Health-Related Quality of Life HRQoL (5). It is the second most common cause of irreversible blindness in the UK, North America and Europe(8,9). The number of patients with glaucoma is predicted to increase substantially as the result of an ageing population(10, 11).

While the incidence and prevalence of glaucoma are commonly reported(11) more granular data regarding the severity of glaucoma at the time of diagnosis is rarely available. In North America, Hattenhauer(12) reported 10% (29/295) of his cohort was blind from glaucoma in at least one eye at diagnosis, while Buys(13) reported 21% (60/290) of a cohort of newly diagnosed glaucoma had severe glaucoma in at least one eye at diagnosis. In the UK the approximately 1 in 4 patients present with advanced disease(14 – 19). , Previous reports from the UK and North America have shown that presentation with advanced glaucoma at diagnosis is more common amongst those people from a poorer socioeconomic back ground(13, 18, 20-23) and it is also recognised that health care usage may be affected by racial or SES background(24 – 25). However, there has been no previous opportunity to specifically look at the characteristics of a large cohort of patients who present with advanced disease or to establish if SES has an effect on treatment outcomes.

Understanding factors that influence the severity of disease presentation in those presenting with already advanced glaucoma is important as presentation with advanced glaucoma is a major risk factor for lifetime blindness and those presenting with advanced glaucoma are those most at risk of developing blindness in their

lifetime(26 – 32). Understanding if there is an effect of SES on treatment outcomes is important as it may influence the choice of treatment recommended.

Effective treatment for glaucoma stops or delays disease progression(33). The Treatment of Advanced Glaucoma Study (TAGS) is a pragmatic randomised controlled trial (RCT) designed to determine whether primary medicine or primary surgery is more effective for patients presenting with advanced glaucoma(34, 35).

The TAGS study has provided an opportunity to evaluate at a more granular level the SES and racial background of those who present with advanced glaucoma in a large cohort of advanced glaucoma patients. It also provides an opportunity to explore these factors on the outcomes of treatment which has not been previously undertaken.

The aim of this report therefore is to explore the effect of SES on quality of life and clinical measures for those presenting with advanced glaucoma and to explore whether SES affects the effectiveness of either medical or surgical management in these patients at 24 months.

Methods

TAGS is a pragmatic multicentre RCT; the design of the study has been described in detail elsewhere(34). Briefly, eligible patients with advanced POAG in either eye were randomised to have augmented trabeculectomy or IOP lowering drops as their primary intervention and followed up for 24 months. Randomisation was based on the participant (not the eye), for those where both eyes were eligible, clinical outcomes are based on the index eye defined as the eye with better mean deviation (MD) value. Research was undertaken in compliance with the tenents of the Declaration of Helsinki and Ethics for this research granted by East Midlands – Derby Research Ethics Committee (reference number 13/EM/0395).

Disease Classification: Eligible patients had primary open angle glaucoma (including pigment dispersion and pseudoexfoliation). Advanced glaucoma was defined according to the Hodapp-Parrish-Anderson (HPA) classification of glaucoma(36). The HPA classification is commonly used in glaucoma research and uses both the position and extent of visual field loss to categorise severity(36). Advanced disease was classified according to the "severe" category of visual field loss using the HPA classification [has **any** of the following]:

1. Mean Deviation (MD) < -12.00dB
2. More than 50% of points depressed below the 5% level on the pattern deviation probability plot
3. More than 20 points depressed below the 1% level on the pattern deviation probability plot
4. A point in the central five degrees has a sensitivity of 0-dB
5. Points within five degrees of fixation under 15 dB sensitivity in both upper and lower hemi-fields.

Outcome Measures: At baseline clinical measurements (visual field loss Mean Deviation VFMD), Logarithm of the mean angle of resolution (logMAR) visual acuity (VA), intraocular pressure (IOP), incidence of blindness(37), family history of glaucoma and self-reported frequency of contact with primary care optometry in years prior to diagnosis were recorded. In addition, Health Related Quality of Life (HRQoL) generic health status [EuroQual-5 dimension – 5 level (EQ-5D-5L)](38) and Health Utility Index (HUI-3)(39), visual health status [National Eye Institute Visual Function Questionnaire 25 (VFQ-25)](40), glaucoma health status [glaucoma utility index (GUI)](41) and patient experience were also recorded at baseline. Outcomes examined and reported at 24 months were VFMD, logMAR VA, IOP and HRQoL.

SES was defined using the Index of Multiple Deprivation (IMD). The IMD is the official measure of relative deprivation for small areas in England. The IMD ranks every small area in England based on postcode from 1 (most deprived area) to 32,844 (least deprived area). The IMD combines information from the seven domains (Income Deprivation, Employment Deprivation, Education, Skills and Training Deprivation, Health Deprivation and Disability, Crime, Barriers to Housing and Services and Living Environment Deprivation) to produce an overall relative measure of deprivation (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/853811/IoD2019_FAQ_v4.pdf).

Statistical analysis: Baseline characteristics are described using numbers and percentages for dichotomous variables, numbers, median and interquartile range (IQR) for the number of times the participant visited the optometrist in the last 10 years and mean and standard deviation (SD) for all remaining continuous variables. For participants in whom both eyes were eligible, data are summarised for both the index and non-index eye. The Chi-squared test of association was used to assess

correlation between IMD scores derived from participants' postcodes and dichotomous variables (gender, ethnicity and family history), and Pairwise Pearson's correlation for continuous variables. As TAGS recruited from England, Scotland and Northern Ireland, we used the Abel et al method to convert the IMD to be on the same scale centred on English scores as 89% of participants were recruited in England(42), IMD is reported in quintiles from 1 (most deprived) through to 5 (least deprived). EQ-5D-5L was calculated following the method by Van Hout et al(43) and GUI was calculated following the method by Burr et al(41). Outcomes at 24 months were analysed using mixed effects linear model correcting for baseline score, bilateral disease and including a random effect for surgery and treatment using restricted maximum likelihood following the partially nested heteroscedastic method by Candlish et at(44) Subgroup analysis explored treatment effect modifications of IMD on IOP, logMAR, VFMD, NEI-VFQ-25, HUI-3 and GUI at 24 months. We used a stricter level of significance (two-sided 1% significance level) and 99% CIs. Subgroup by treatment interaction was assessed by included interaction terms in the model outlined above. Due to imbalances between IMD group as baseline for gender, age and ethnicity a sensitivity analysis adjusted for these covariates. As conclusions did not change, results are not provided. Outcomes by IMD were also analysed using linear regression adjusting for baseline score for overall cohort and by treatment arm at 24 months. All analyses were performed in Stata 16 software. (45)

Results

All patient recruited to TAGS had advanced glaucoma in at least one eye according to the Hodapp classification at diagnosis. The IMD quintiles for the randomised participants were roughly equal between the two treatment arms (Supplementary Table 1) and across each quintile.

Table 1 shows the patient characteristic values for baseline data for each quintile of deprivation for the whole cohort. It can be seen that on average there is nearly an eight-year difference in age of diagnosis between those in the lowest and highest deprivation groups with those in the most deprived group being younger. Similarly, there is a much higher proportion of non-Caucasian patients in the lower socioeconomic groups.

For patient reported outcomes, there is a 5-point difference between the upper and lower quintiles for composite vision specific VFQ score. This is represented most markedly in the near activities, dependency, driving, general health, role difficulties, mental health, general vision and ocular pain domains. There was no material difference for either of the generic HRQoL measures or the glaucoma specific GUI between quintiles.

Table 2 reports the baseline clinical characteristics and IMD for the index eye. It can be seen that on average those in the lowest SE quintile have 4dB more VF loss at presentation than those with highest SES. Similarly, those in the lowest quintile have on average a higher IOP by about 4mmHg at diagnosis. Similar observations are made for the non-index eye (supplementary Table 2). The IOP was highest at diagnosis in the lowest SES quintile, the lower IOP noted in quintile 5 is a reflection that a higher proportion of patients presented with IOP < 22mmHg (IOP<22mmHG, 29, 29,27,29,35% for quintiles 1 – 5 respectively) suggesting a higher proportion of normal tension glaucoma in this group. However, at baseline (following initial medications) the

IOP is reduced to a similar level across the quintile spectrum for both index and non-index eyes.

Table 3 shows that the SES differences at baseline are highly statistically significant for age, ethnicity, number of visits to optometrists, vision specific health (VFQ-25) and visual field MD for both the index and non-index eye.

Subgroup analysis for IOP, VF MD and logMAR visual acuity and QoL measures at 24 months are shown in Figure 1 and Supplementary Figure 1. The trabeculectomy arm had lower IOP for all IMD quintile groups with the biggest difference for the second (MD -3.67 95% CI (-7.05, -0.30); p-value 0.005) and third quintile (MD -3.67, 95% CI (-6.68, -0.83); p-value 0.001. However, there was no evidence that the treatment effect was moderated by the quintiles. There was no material difference for VA or VF loss between the trabeculectomy or medical management arms based on IMD score and no evidence that the treatment effect was moderated by the quintiles (Figure 1). Subgroup analysis for IMD and quality of life at 24 months showed there was no evidence that the treatment effect was moderated by the quintiles (Supplementary Figure 1)

There were no material differences between quintiles for outcomes based on intervention either for the cohort as a whole (Supplementary Table 3) or for either the trabeculectomy or medical management arms (Tables 4).

Discussion

TAGS was designed to be a pragmatic trial comparing established options, medications or surgery, as initial treatment for people diagnosed with severe glaucoma. Only the primary intervention was dictated by the trial protocol(34). The effect of SES on health outcomes is well recognised in terms of mortality(1) and for specific diseases such as cancer(1, 46 – 51) and cardiovascular disease(52, 53), with those from more deprived backgrounds having poorer outcomes.

TAGS is the largest RCT comparing treatments for advanced glaucoma and offered a unique opportunity to explore how outcomes for patients with advanced glaucoma are affected by SES and whether there is a difference of outcomes based on SES for medical or surgical interventions. In addition, the large number of patients, all with advanced glaucoma provided a unique opportunity for a more in-depth exploration of the effects of SES on patients presenting with advanced glaucoma using prospectively collected data in a representative sample of a population with advanced glaucoma(54). The analysis used participants' postcode as a proxy for SES to look at this important dimension *within* those presenting with advanced disease.

Several previous studies have similarly indicated that for glaucoma advanced presentation compared to non-advanced disease is linked to poorer socioeconomic status(18, 20-22), however unlike TAGS this has been data collected from retrospectively evaluated cohorts.

At baseline in our cohort, poorer socioeconomic background correlates with more advanced disease at presentation in terms of visual field loss in the index and non-index eye, indicating that the relationship between more advanced visual field loss and poorer SES exists even in a cohort with advanced glaucoma and is present in both eyes. This may explain the correlation between poorer socioeconomic status and poorer vision related QoL,the subscales most affected are those of near activities, role

limitation and dependency. Near activities refer to limited ability to read small print and undertake some personal tasks such as shaving and putting on makeup which require near vision clarity. Role limitations refers to requirement for more help from others in undertaking everyday tasks and limiting activities because of vision and dependency specifically refers to limiting activity outside the home because of vision (Table 1). It is reasonable to assume that these activities will be affected by more advanced visual field loss particularly when affecting both eyes(55). It is likely that patients with advanced glaucoma have some awareness of vision deterioration especially if affecting both eye(55). One possibility that this reduced vision may not have prompted patients to seek attention earlier, is a resignation among older people that poorer vision is a natural consequence of ageing(56) and they may not therefore pay much attention to the subtle and slowly developing deterioration associated with visual field loss, especially if only affecting one eye. Previous studies have identified older age(19, 20) and ethnicity as risk factors for presentation with advanced glaucoma. However further evaluation of this in the TAGS cohort of patients presenting with advanced disease reveals that patients with lower SES are younger, have more advanced disease at presentation in both eyes and are more commonly from a non-Caucasian ethnic background. This is important in terms of lifetime vision loss prevention as those patients with the most severe vision loss are most likely to lose vision during their lifetime even with treatment and as these patients are the youngest they are more likely to spend a longer period of their life with severe visual disability. Indeed over 6% of the cohort were eligible for sight impairment registration at the time of diagnosis(37) and 10.6% did not achieve the visual standards for driving, once again these were seen more commonly in those with lower SES.

One mechanism for minimising risk of presentation with advanced glaucoma is a regular visit to an eye care professional. In England, current policy facilitates visits to a community optometrist annually for those over 40 years with a family history of glaucoma. In TAGS, there is a correlation between fewer visits to the optician in the

previous 10 years and SES. In the UK and many countries glaucoma diagnosis is a consequence of opportunistic case finding, fewer visits means less opportunity for those of lower SES to have their glaucoma picked up through routine optometrist eyes visits, thus resulting in more advanced presentation. Indeed, Shickle (57) observed that "A person aged 60 or over living in the least deprived quintile is 71% more likely to attend for an eye examination than someone in that age group in the most deprived quintile in Leeds, even though both have the same entitlement". This may be representative of the UK as a whole explaining this observation. The reason these opportunities to diagnose glaucoma earlier are missed is unknown. Several possibilities exist, It is possible that even though entitlement is equal for all SES groups the messaging around need to attend for routine testing or awareness of these services may be less for those from lower SES groups(58 – 60) and therefore improved awareness and education of those at risk may help to overcome this. It is also possible that participants have some recall bias and over-estimated the frequency of visits to their optometrists prior to diagnosis or that they were rapid progressors as previously suggested by Fraser(20). It has also been suggested that delays in diagnosis may occur at several distinct points in a patient pathway, from failure of recognition/diagnosis of glaucoma by optometrists, to failure to refer appropriately or delays in this process occurring(61).

Nearly one third of our cohort reported a family history of glaucoma which is similar to three previous primary intervention studies of patients with early glaucoma(62-64), suggesting that having a family history of glaucoma does not reduce your risk of presenting with advanced disease. This is a disappointing observation as in the UK patients 40 years of age with a family history of glaucoma are entitled to a free glaucoma screening eye exam annually and it would be hoped that this would reduce the risk of presenting with advanced disease.

These findings suggest that, despite a robust public health provision in the UK to prevent diagnosis with advanced disease, a large number of patients are still not being

diagnosed at an early stage and this disproportionally affects those from poorer SES backgrounds who have more severe visual field loss and more reduction in visual QoL at diagnosis. Addressing this should be a research priority.

TAGS employed two current standard interventions for lowering IOP. There was no difference between SES quintiles in outcomes at 24 months for the cohort as a whole (Supplementary Table 3). There was a significant difference between treatment arms for the IOP measurement for all quintiles of SES, however this difference did not appear to vary between different quintiles of SES and represents the general difference in IOP lowering achieved in the study between the medical and surgical arms of the study (Figure 1). There was no difference in any outcomes between quintiles within either the medically treated arm or the trabeculectomy arm of the study. It is not surprising following surgery that IOP remains relatively equivalent between quintiles as there is generally no reliance on further treatment delivered by the patient, however in the medicine group a reliance on use of drops remains and is ongoing. Adherence is a recognised problem for glaucoma patients using drops(65) and poorer adherence is corelated with greater glaucoma progression(66). Both age and educational achievement have been implicated as barriers to adherence(65) and these differ between the quintiles of the medical arm of the TAGS cohort, potentially leading to a difference in adherence to drops(67). However, there is no difference detected in IOP between quintiles in the TAGS medical arm to suggest that SES has an influence on the level of IOP achieved and maintained.

In conclusion in patients presenting with advanced glaucoma, SES influences the severity of presentation with those from lower SES having more advanced visual field loss in both eyes at presentation and worse vision related quality of life, they also tend to be younger and more commonly from non-Caucasian ethnicity. Following treatment

SES does not appear to influence the success of either medical or surgical outcomes at 24 months.

Competing Interest Statement

None of the authors have any competing interests relating to this project

Contributorship Statement

AJK - study design, data collection, manuscript writing and review,

JH - study design, data analysis, manuscript writing and review

AAB - study design, data collection, manuscript review,

GMc - study design, data analysis, manuscript review

JK - study design, data collection, manuscript review

SG - study design, data collection, manuscript review

SL - study design, data collection, manuscript review

All authors confirm approval of final submitted manuscript

Ethics Statement

Ethics for this research granted by East Midlands – Derby Research Ethics Committee (reference number 13/EM/0395).

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Table 1. Baseline characteristics by IMD for overall cohort

	IMD 1 N=106	IMD 2 N=67	IMD 3 N=88	IMD 4 N=93	IMD 5 N=96
Age - mean (SD); n	62.3 (14.4); 106	66.0 (12.3); 67	68.0 (11.5); 88	69.5 (10.8); 93	70.1 (10.6); 96
Gender - n (%)					
Male	77 (72.6)	49 (73.1)	56 (63.6)	58 (62.4)	60 (62.5)
Female	29 (27.4)	18 (26.9)	32 (36.4)	35 (37.6)	36 (37.5)
Ethnicity - n (%)					
Caucasian	61 (57.5)	50 (74.6)	75 (85.2)	90 (96.8)	94 (97.9)
Afro-Caribbean	36 (34.0)	12 (17.9)	8 (9.1)	3 (3.2)	0 (0)
Asian - India/Pakistan/Bangladesh	5 (4.7)	3 (4.5)	3 (3.4)	0 (0)	1 (1.0)
Asian - Oriental	0 (0)	1 (1.5)	1 (1.1)	0 (0)	0 (0)
Mixed heritage	0 (0)	0 (0)	1 (1.1)	0 (0)	0 (0)
Other	3 (2.8)	1 (1.5)	0 (0)	0 (0)	1 (1.0)
Missing	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)
Advanced glaucoma in both eyes - n (%)					
No	88 (83.0)	45 (67.2)	64 (72.7)	78 (83.9)	87 (90.6)
Yes	18 (17.0)	22 (32.8)	24 (27.3)	15 (16.1)	9 (9.4)
Glaucoma in both eyes – n (%)					
No	20 (18.9)	13 (19.4)	19 (21.6)	26 (28.0)	26 (27.1)
Yes	86 (81.1)	54 (80.6)	69 (78.4)	67 (72.0)	70 (72.9)
Eligible to be registered as sight impaired - n (%)					
No	97 (91.5)	57 (85.1)	84 (95.5)	92 (98.9)	93 (96.9)

Sight impaired	8 (7.5)	9 (13.4)	2 (2.3)	1 (1.1)	2 (2.1)
Severe sight impaired	1 (0.9)	1 (1.5)	2 (2.3)	0 (0)	1 (1.0)
Glaucoma diagnosis - n (%)					
Primary open angle glaucoma (including NTG)	105 (99.1)	61 (91.0)	85 (96.6)	92 (98.9)	93 (96.9)
Pigment dispersion syndrome	0 (0)	2 (3.0)	3 (3.4)	1 (1.1)	3 (3.1)
Psuedoexfoliation syndrome	1 (0.9)	4 (6.0)	0 (0)	0 (0)	0 (0)
Family history of glaucoma - n (%)					
Yes	35 (33.0)	12 (17.9)	31 (35.2)	29 (31.2)	34 (35.4)
No	67 (63.2)	48 (71.6)	54 (61.4)	58 (62.4)	55 (57.3)
Missing	4 (3.8)	7 (10.4)	3 (3.4)	6 (6.5)	7 (7.3)
Number of times visited the optician in the last 10 year – median [IQR]; n	4 [2, 5]; 98	5 [2.5, 10]; 60	4 [2, 6]; 86	5 [3, 8]; 85	5 [4, 7]; 91
NEI-VFQ-25 - mean (SD); n	83.9 (15.8); 104	81.5 (16.2); 66	89.6 (11.5); 88	89.5 (11.2); 93	89.5 (10.7); 96
NEI-VFQ-25 subscales - mean (SD); n					
Near activities	80.6 (21.8); 103	79.5 (17.6); 66	86.7 (16.8); 88	87.9 (13.8); 93	85.6 (16.0); 96
Distance activities	87.6 (18.2); 104	83.1 (17.6); 66	91.7 (12.9); 88	90.3 (13.9); 93	91.0 (12.3); 96
Dependency	90.7 (21.2); 104	91.3 (21.7); 65	97.0 (10.7); 87	96.0 (12.6); 93	96.8 (13.6); 96
Driving	82.6 (32.6); 65	71.2 (37.4); 37	89.8 (18.5); 70	87.7 (24.1); 73	88.1 (20.8); 81
General health	57.3 (25.6); 103	60.4 (22.5); 65	63.4 (21.1); 88	62.1 (22.9); 93	67.7 (21.4); 96
Role difficulties	83.1 (22.2); 104	80.6 (24.7); 65	89.7 (16.1); 87	90.2 (19.3); 93	91.0 (17.5); 96

Mental health	75.0 (24.4); 104	73.2 (25.1); 66	84.9 (14.9); 88	86.0 (16.6); 93	86.1 (17.3); 96
General vision	69.9 (15.7); 101	69.7 (14.6); 66	76.6 (14.0); 88	77.4 (12.9); 93	74.7 (13.1); 95
Social function	94.1 (13.5); 104	90.5 (15.4); 66	95.9 (12.1); 88	96.7 (9.1); 92	96.7 (9.1); 96
Colour vision	94.5 (14.8); 104	94.9 (11.9); 64	98.3 (10.0); 86	97.8 (8.0); 92	97.9 (8.6); 96
Peripheral vision	85.1 (22.2); 104	80.8 (24.5); 65	89.2 (19.3); 88	88.6 (19.0); 92	88.8 (17.3); 96
Ocular pain	79.7 (21.4); 103	80.3 (19.6); 66	88.1 (16.0); 88	86.0 (16.7); 93	86.8 (15.0); 96
EQ-5D-5L - mean (SD); n	0.827 (0.219); 101	0.820 (0.157); 65	0.862 (0.171); 88	0.838 (0.168); 92	0.852 (0.173); 95
HUI-3 - mean (SD); n	0.803 (0.248); 98	0.789 (0.187); 61	0.830 (0.200); 84	0.808 (0.202); 90	0.820 (0.175); 92
GUI - mean (SD); n	0.883 (0.148); 101	0.857 (0.124); 63	0.902 (0.114); 86	0.899 (0.119); 93	0.905 (0.103); 96
Participant experience (glaucoma getting worse) - n (%)					
Yes	42 (39.6)	31 (46.3)	27 (30.7)	35 (37.6)	36 (37.5)
No	56 (52.8)	30 (44.8)	53 (60.2)	51 (54.8)	54 (56.3)
Missing	8 (7.5)	6 (9.0)	8 (9.1)	7 (7.5)	6 (6.3)
Visual standards for driving - n (%)					
Pass	89 (84.0)	50 (74.6)	73 (83.0)	81 (87.1)	87 (90.6)
Fail	12 (11.3)	14 (20.9)	12 (13.6)	5 (5.4)	5 (5.2)
Missing	5 (4.7)	3 (4.5)	3 (3.4)	7 (7.5)	4 (4.2)
Diamox[A]- n (%)	5 (4.7)	1 (1.5)	2 (2.3)	0 (0)	0 (0)

[A]taken orally. SD standard deviation

Table 2. Baseline clinical characteristics for index eye for overall cohort

	IMD 1 N=106	IMD 2 N=67	IMD 3 N=88	IMD 4 N=93	IMD 5 N=96
Lens status - n (%)					
Phakic	100 (94.3)	64 (95.5)	82 (93.2)	84 (90.3)	88 (91.7)
Pseudophakic	6 (5.7)	3 (4.5)	6 (6.8)	9 (9.7)	8 (8.3)
Central corneal thickness - - mean (SD); n	541.7 (38.5); 105	543.1 (33.5); 67	540.9 (36.3); 86	537.9 (33.9); 93	539.3 (35.9); 95
Glaucoma drops - n (%)					
Pg analogue	89 (84.0)	54 (80.6)	73 (83.0)	72 (77.4)	77 (80.2)
β-blocker	31 (29.2)	26 (38.8)	21 (23.9)	9 (9.7)	17 (17.7)
CA inhibitor	23 (21.7)	20 (29.9)	16 (18.2)	9 (9.7)	10 (10.4)
Agonist	6 (5.7)	2 (3.0)	0 (0)	2 (2.2)	1 (1.0)
Ocular co-morbidity - n (%)					
Yes	17 (16.0)	13 (19.4)	23 (26.1)	23 (24.7)	24 (25.0)
No	89 (84.0)	54 (80.6)	65 (73.9)	70 (75.3)	72 (75.0)
Ocular co-morbidity details [A]					
AMD	1 (5.9)	2 (15.4)	4 (17.4)	1 (4.3)	2 (8.3)
Cataract	12 (70.6)	11 (84.6)	19 (82.6)	21 (91.3)	21 (87.5)
Vascular occlusion	1 (5.9)	0 (0)	1 (4.3)	1 (4.3)	0 (0)
Diabetic retinopathy	2 (11.8)	0 (0)	0 (0)	0 (0)	0 (0)
Other	1 (5.9)	2 (15.4)	2 (8.7)	6 (26.1)	4 (16.7)
LogMAR visual acuity - mean (SD); n	0.2 (0.4); 105	0.1 (0.2); 66	0.1 (0.2); 88	0.1 (0.2); 92	0.2 (0.2); 96

Visual fields mean deviation (dB) - mean (SD); n	-17.2 (6.7); 106	-16.9 (6.6); 67	-15.3 (5.4); 88	-13.5 (6.4); 93	-13.0 (5.5); 96
Intraocular pressure (mmHg) - mean (SD); n					
Diagnosis	28.2 (10.6); 105	27.1 (9.0); 66	26.6 (9.0); 88	25.8 (7.2); 92	24.5 (7.1); 95
Baseline	19.0 (5.8); 105	19.8 (6.5); 67	19.2 (5.3); 86	20.1 (6.6); 88	18.4 (5.4); 94

[A]participants can have more than one. SD standard deviation

Table 3 - Index of Multiple Deprivation correlations for overall cohort

	Index of Multiple Deprivation	
	Pearson's correlation	p-value
Gender		0.30
Ethnicity		<0.001
Family history of glaucoma		0.19
Age	0.23	<0.001
Number of times visited the optician in the last 10 year	0.10	0.028
NEI-VFQ-25	0.19	<0.001
EQ-5D-5L	0.05	0.29
HUI-3	0.03	0.48
GUI	0.09	0.06
LogMAR visual acuity for index eye	-0.12	0.014
Log MAR visual acuity for non-index eye	-0.02	0.75
Log MAR f visual acuity or both eyes combined	0.02	0.69
Visual fields mean deviation (dB) for index eye	0.27	<0.001
Visual fields mean deviation (dB) for non-index eye	0.23	<0.001
Intraocular pressure (mmHg) for index eye	-0.02	0.64

Chi-squared test for association was used for dichotomous variables and Pearson's correlation with p-value for continuous

Table 4 - difference in the outcome by IMD for participants randomised to trabeculectomy and medical treatment

Trabeculectomy					
	Baseline	24 months	Interaction	95% CI	p-value
Glaucoma drops					
IMD 1	1.41 (0.94); 54	0.55 (0.94); 51			
IMD 2	1.50 (1.25); 30	0.73 (1.12); 26	0.15	(-0.27, 0.58)	0.480
IMD 3	1.24 (0.93); 45	0.41 (0.87); 41	-0.11	(-0.49, 0.26)	0.546
IMD 4	1.04 (0.81); 50	0.33 (0.94); 46	-0.18	(-0.55, 0.18)	0.319
IMD 5	1.28 (0.85); 47	0.43 (0.78); 46	-0.09	(-0.45, 0.27)	0.618
IOP (mmHg)					
IMD 1	18.94 (6.27); 51	13.45 (5.57); 50			
IMD 2	20.69 (7.94); 26	12.24 (4.09); 25	-1.39	(-3.61, 0.83)	0.220
IMD 3	19.65 (5.75); 41	11.02 (3.76); 39	-2.50	(-4.43, -0.57)	0.011
IMD 4	20.33 (5.85); 46	12.38 (4.67); 46	-1.19	(-3.04, 0.66)	0.207
IMD 5	18.16 (5.72); 46	12.61 (4.69); 45	-0.78	(-2.64, 1.07)	0.409
VF MD (dB)					
IMD 1	-16.11 (6.16); 51	-16.11 (6.66); 50			
IMD 2	-19.00 (6.44); 26	-18.68 (6.02); 24	-0.54	(-1.97, 0.88)	0.454
IMD 3	-15.67 (5.43); 41	-15.72 (5.54); 39	0.06	(-1.16, 1.28)	0.918
IMD 4	-12.80 (6.68); 46	-13.31 (7.05); 44	0.01	(-1.18, 1.21)	0.982
IMD 5	-12.53 (5.55); 46	-13.53 (6.60); 44	-0.79	(-2.00, 0.41)	0.196
LogMAR visual acuity					
IMD 1	0.20 (0.35); 51	0.22 (0.31); 49			
IMD 2	0.14 (0.15); 26	0.21 (0.32); 24	0.02	(-0.09, 0.14)	0.687
IMD 3	0.15 (0.26); 41	0.22 (0.29); 38	0.02	(-0.09, 0.12)	0.730
IMD 4	0.07 (0.16); 46	0.23 (0.29); 45	0.07	(-0.03, 0.17)	0.153
IMD 5	0.13 (0.19); 46	0.19 (0.19); 42	0.02	(-0.08, 0.12)	0.743
NEI-VFQ-25					
IMD 1	82.39 (16.00); 50	81.91 (15.82); 50			
IMD 2	82.82 (16.72); 26	80.41 (15.32); 26	-1.78	(-6.54, 2.98)	0.463

IMD 3	88.56 (13.36); 40	83.71 (16.52); 40	-2.30	(-6.52, 1.93)	0.287
IMD 4	91.10 (9.33); 47	88.93 (10.64); 46	1.21	(-2.92, 5.33)	0.566
IMD 5	90.83 (10.78); 44	90.20 (7.85); 44	2.67	(-1.49, 6.84)	0.208
EQ-5D-5L					
IMD 1	0.81 (0.24); 50	0.78 (0.21); 50			
IMD 2	0.83 (0.18); 26	0.80 (0.17); 25	0.02	(-0.05, 0.08)	0.582
IMD 3	0.85 (0.18); 40	0.81 (0.22); 40	0.01	(-0.05, 0.07)	0.761
IMD 4	0.87 (0.13); 47	0.84 (0.14); 46	0.03	(-0.02, 0.09)	0.252
IMD 5	0.87 (0.18); 44	0.82 (0.15); 44	0.01	(-0.05, 0.06)	0.784
HUI-3					
IMD 1	0.79 (0.24); 50	0.76 (0.26); 46			
IMD 2	0.79 (0.21); 26	0.76 (0.27); 24	0.00	(-0.08, 0.09)	0.928
IMD 3	0.80 (0.24); 40	0.75 (0.28); 38	-0.01	(-0.08, 0.07)	0.844
IMD 4	0.84 (0.15); 47	0.83 (0.17); 45	0.03	(-0.04, 0.11)	0.375
IMD 5	0.85 (0.13); 44	0.81 (0.17); 44	0.01	(-0.07, 0.08)	0.868
GUI					
IMD 1	0.87 (0.15); 50	0.85 (0.17); 50			
IMD 2	0.88 (0.11); 26	0.81 (0.16); 26	-0.04	(-0.11, 0.02)	0.171
IMD 3	0.89 (0.14); 40	0.82 (0.19); 39	-0.04	(-0.10, 0.01)	0.142
IMD 4	0.92 (0.11); 47	0.91 (0.10); 46	0.03	(-0.02, 0.08)	0.277
IMD 5	0.93 (0.10); 44	0.89 (0.10); 43	0.02	(-0.04, 0.07)	0.543

Medical Management

	Baseline	**24 months**	**Interaction**	**95% CI**	**p-value**
Glaucoma drops					
IMD 1	1.40 (1.16); 52	1.68 (1.22); 44			
IMD 2	1.54 (0.77); 37	2.00 (1.10); 34	0.29	(-0.22, 0.80)	0.261
IMD 3	1.26 (0.76); 43	1.40 (1.15); 40	-0.27	(-0.76, 0.21)	0.274
IMD 4	0.93 (0.70); 43	1.71 (1.13); 42	0.07	(-0.41, 0.56)	0.773
IMD 5	0.92 (0.61); 49	1.46 (1.13); 46	-0.19	(-0.66, 0.29)	0.440
IOP (mmHg)					
IMD 1	18.43 (4.17); 44	15.32 (3.32); 43			
IMD 2	19.29 (5.62); 34	15.92 (7.91); 34	0.46	(-1.65, 2.57)	0.672
IMD 3	19.04 (4.95); 40	14.78 (3.84); 38	-0.65	(-2.69, 1.40)	0.537
IMD 4	20.18 (7.53); 42	14.85 (4.56); 40	-0.71	(-2.74, 1.31)	0.490
IMD 5	18.30 (5.18); 46	14.72 (3.96); 45	-0.60	(-2.55, 1.36)	0.551

VF MD (dB)					
IMD 1	-18.56 (6.87); 44	-17.26 (6.85); 41			
IMD 2	-15.56 (6.05); 34	-16.72 (6.06); 34	-1.45	(-2.99, 0.10)	0.066
IMD 3	-14.49 (5.61); 40	-14.96 (5.97); 38	-1.01	(-2.53, 0.50)	0.190
IMD 4	-13.99 (6.13); 42	-14.47 (7.20); 40	-0.64	(-2.14, 0.87)	0.406
IMD 5	-12.94 (5.48); 46	-13.99 (5.55); 45	-1.05	(-2.53, 0.43)	0.164
LogMAR visual acuity					
IMD 1	0.24 (0.39); 44	0.22 (0.38); 42			
IMD 2	0.13 (0.22); 34	0.14 (0.19); 33	-0.02	(-0.10, 0.06)	0.639
IMD 3	0.14 (0.21); 40	0.14 (0.17); 38	-0.01	(-0.09, 0.07)	0.770
IMD 4	0.16 (0.18); 42	0.18 (0.27); 41	-0.01	(-0.08, 0.07)	0.867
IMD 5	0.17 (0.20); 46	0.13 (0.20); 45	-0.06	(-0.13, 0.01)	0.104
NEI-VFQ-25					
IMD 1	86.21 (15.23); 42	86.25 (15.36); 42			
IMD 2	81.00 (16.09); 34	77.40 (19.71); 34	-4.15	(-9.26, 0.95)	0.111
IMD 3	90.80 (10.08); 39	86.47 (13.26); 39	-3.92	(-8.83, 1.00)	0.118
IMD 4	88.82 (11.10); 42	82.55 (19.03); 42	-6.05	(-10.85, -1.24)	0.014
IMD 5	89.52 (10.18); 46	87.66 (12.66); 46	-1.57	(-6.27, 3.13)	0.513
EQ-5D-5L					
IMD 1	0.83 (0.20); 42	0.80 (0.23); 41			
IMD 2	0.83 (0.12); 34	0.77 (0.18); 33	-0.01	(-0.08, 0.06)	0.819
IMD 3	0.89 (0.14); 39	0.84 (0.12); 39	0.02	(-0.05, 0.09)	0.508
IMD 4	0.83 (0.16); 42	0.74 (0.22); 42	-0.04	(-0.11, 0.03)	0.218
IMD 5	0.85 (0.17); 46	0.83 (0.17); 46	0.03	(-0.04, 0.10)	0.387
HUI-3					
IMD 1	0.81 (0.25); 42	0.76 (0.29); 38			
IMD 2	0.80 (0.17); 34	0.74 (0.24); 33	0.01	(-0.07, 0.09)	0.806
IMD 3	0.88 (0.10); 39	0.79 (0.19); 39	-0.00	(-0.08, 0.08)	0.960
IMD 4	0.78 (0.23); 42	0.67 (0.29); 39	-0.03	(-0.11, 0.05)	0.480

	IMD 5	0.81 (0.19); 46	0.79 (0.21); 42	0.05	(-0.03, 0.12)	0.254
GUI						
	IMD 1	0.90 (0.12); 42	0.89 (0.15); 40			
	IMD 2	0.85 (0.11); 34	0.78 (0.19); 34	-0.06	(-0.12, 0.01)	0.086
	IMD 3	0.91 (0.09); 39	0.86 (0.14); 39	-0.03	(-0.09, 0.03)	0.318
	IMD 4	0.88 (0.12); 42	0.82 (0.23); 42	-0.05	(-0.11, 0.01)	0.114
	IMD 5	0.89 (0.10); 46	0.87 (0.14); 45	-0.01	(-0.07, 0.05)	0.692

Values are mean (standard deviation); n. CI Confidence Interval

Figure Legends

Figure 1: Subgroup for Trabeculectomy versus Medical management: (a) IOP; (b) VF MD; (c) logMAR visual acuity

Supplementary Figure 1 – Subgroup for Trabeculectomy versus Medical management: (d) NEI-VFQ-25; (e) EQ-5D-5L; (f) HUI-3; (g) GUI. 1st quintile – most deprived, 5th quintile -least deprived

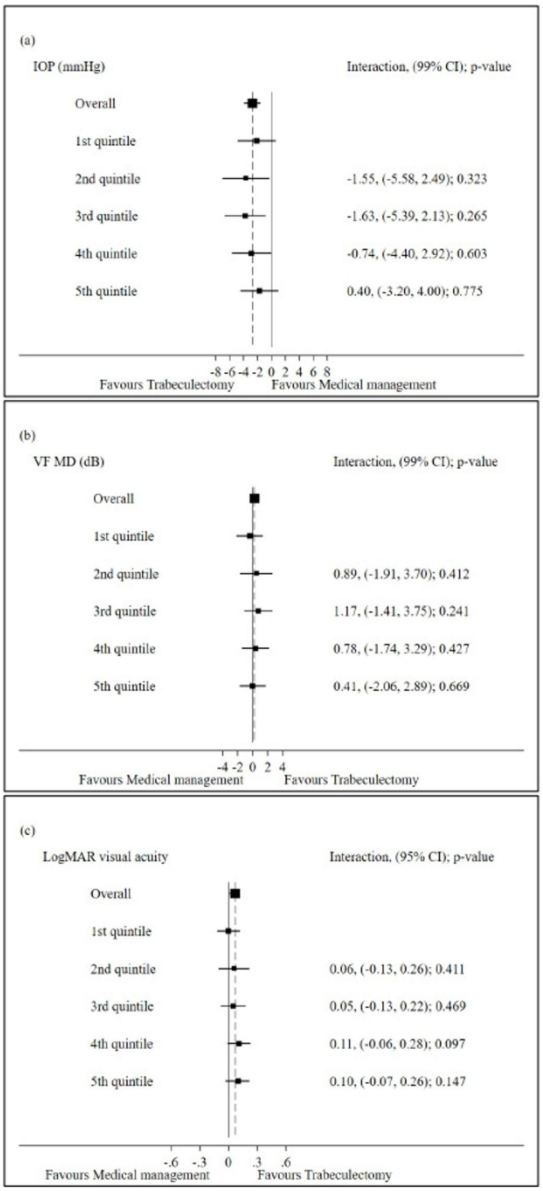


Figure 1: Subgroup for Trabeculectomy versus Medical management: (a) IOP; (b) VF MD; (c) logMAR visual acuity

90x194mm (300 x 300 DPI)

Supplementary Table 1. Index Multiple Deprivation (IMD)

	Trabeculectomy N=227	Medical management N=226
1st quintile (most deprived) (IMD 1)	54 (23.8)	52 (23.0)
2nd quintile (IMD 2)	30 (13.2)	37 (16.4)
3rd quintile (IMD 3)	45 (19.8)	43 (19.0)
4th quintile (IMD 4)	50 (22.0)	43 (19.0)
5th quintile (least deprived) (IMD 5)	47 (20.7)	49 (21.7)
Missing	1 (0.4)	2 (0.9)

Values are numbers (percent).

Supplementary Table 2 - Baseline clinical characteristics for non-index eye for overall cohort by IMD

	IMD 1 N=106	IMD 2 N=67	IMD 3 N=88	IMD 4 N=93	IMD 5 N=96
Lens status - n (%)					
Phakic	99 (93.4)	61 (91.0)	84 (95.5)	83 (89.2)	88 (91.7)
Pseudophakic	6 (5.7)	6 (9.0)	4 (4.5)	10 (10.8)	8 (8.3)
Missing	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)
Central corneal thickness - n; mean (SD)	541.2 (40.9); 104	543.9 (32.5); 67	541.6 (37.9); 86	539.5 (34.7); 93	539.9 (36.9); 95
Glaucoma drops - n (%)					
Pg Analogue	80 (75.5)	46 (68.7)	71 (80.7)	57 (61.3)	64 (66.7)
β-blocker	25 (23.6)	20 (29.9)	18 (20.5)	6 (6.5)	13 (13.5)
CA Inhibitor	13 (12.3)	13 (19.4)	13 (14.8)	7 (7.5)	8 (8.3)
α- Agonist	4 (3.8)	1 (1.5)	0 (0)	1 (1.1)	1 (1.0)
Ocular co-morbidity - n (%)					
Yes	16 (15.1)	14 (20.9)	24 (27.3)	23 (24.7)	21 (21.9)
No	90 (84.9)	53 (79.1)	64 (72.7)	70 (75.3)	75 (78.1)
Ocular co-morbidity details [1]					
AMD	1 (5.9)	2 (15.4)	4 (17.4)	1 (4.3)	2 (8.3)
Cataract	11 (64.7)	11 (84.6)	17 (73.9)	17 (73.9)	19 (79.2)
Diabetic retinopathy	2 (11.8)	0 (0)	0 (0)	0 (0)	0 (0)
Other	1 (5.9)	1 (7.7)	5 (21.7)	7 (30.4)	2 (8.3)
LogMAR visual acuity - mean (SD); n	0.1 (0.2); 105	0.1 (0.3); 65	0.1 (0.3); 87	0.1 (0.2); 92	0.1 (0.2); 96
Visual fields mean deviation (dB) - mean (SD); n	-7.4 (8.2); 104	-9.2 (9.3); 67	-6.7 (7.7); 88	-4.4 (5.6); 93	-3.9 (4.9); 96
Intraocular pressure (mmHg) - mean (SD); n					
Diagnosis	24.1 (7.9); 104	24.2 (8.9); 66	23.3 (6.8); 88	22.3 (6.0); 92	21.0 (5.0); 95
Baseline	18.0 (4.7); 104	18.6 (6.0); 67	17.8 (4.4); 86	18.1 (4.1); 88	17.4 (4.2); 94

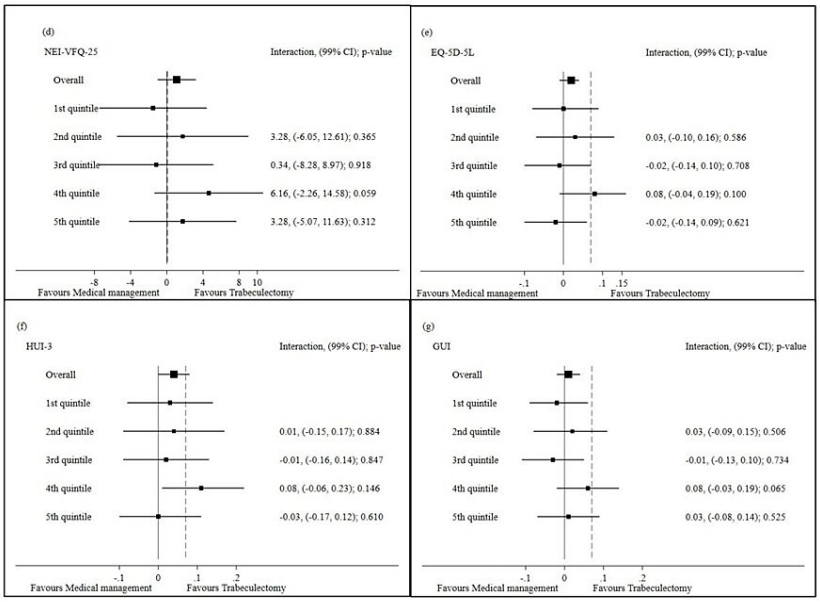
[1]participants can have more than one. SD standard deviation

Supplementary Table 3 - difference in the outcome by IMD for the overall cohort

	Baseline	24 months	Interaction	95% CI	p-value
Glaucoma drops					
IMD 1	1.41 (1.05); 106	1.07 (1.21); 95			
IMD 2	1.52 (1.01); 67	1.45 (1.27); 60	0.36	(-0.02, 0.75)	0.063
IMD 3	1.25 (0.85); 88	0.90 (1.12); 81	-0.16	(-0.51, 0.19)	0.357
IMD 4	0.99 (0.76); 93	0.99 (1.25); 88	-0.07	(-0.41, 0.28)	0.712
IMD 5	1.09 (0.76); 96	0.95 (1.09); 92	-0.11	(-0.45, 0.23)	0.519
IOP (mmHg)					
IMD 1	18.70 (5.38); 95	14.31 (4.73); 93			
IMD 2	19.90 (6.70); 60	14.36 (6.78); 59	-0.10	(-1.69, 1.49)	0.902
IMD 3	19.35 (5.35); 81	12.87 (4.22); 77	-1.52	(-2.99, -0.05)	0.043
IMD 4	20.26 (6.67); 88	13.53 (4.76); 86	-0.94	(-2.37, 0.49)	0.197
IMD 5	18.23 (5.42); 92	13.66 (4.44); 90	-0.61	(-2.02, 0.80)	0.398
VF MD (dB)					
IMD 1	-17.24 (6.58); 95	-16.63 (6.73); 91			
IMD 2	-17.05 (6.40); 60	-17.53 (6.07); 58	-1.06	(-2.10, -0.02)	0.045
IMD 3	-15.09 (5.52); 81	-15.34 (5.73); 77	-0.48	(-1.44, 0.49)	0.331
IMD 4	-13.37 (6.41); 88	-13.87 (7.10); 84	-0.28	(-1.23, 0.67)	0.564
IMD 5	-12.74 (5.49); 92	-13.77 (6.06); 89	-0.90	(-1.85, 0.05)	0.062
LogMAR visual acuity					
IMD 1	0.21 (0.37); 95	0.22 (0.34); 91			
IMD 2	0.13 (0.19); 60	0.17 (0.25); 57	-0.00	(-0.08, 0.07)	0.911
IMD 3	0.14 (0.23); 81	0.18 (0.24); 76	-0.00	(-0.07, 0.07)	0.972
IMD 4	0.11 (0.17); 88	0.20 (0.28); 86	0.04	(-0.03, 0.10)	0.241
IMD 5	0.15 (0.19); 92	0.16 (0.20); 87	-0.02	(-0.09, 0.04)	0.497
NEI-VFQ-25					
IMD 1	84.13 (15.69); 92	83.89 (15.68); 92			
IMD 2	81.79 (16.25); 60	78.70 (17.86); 60	-3.35	(-6.87, 0.17)	0.062
IMD 3	89.66 (11.83); 79	85.08 (14.97); 79	-3.15	(-6.43, 0.13)	0.060
IMD 4	90.02 (10.21); 89	85.89 (15.48); 88	-2.62	(-5.82, 0.57)	0.108
IMD 5	90.16 (10.44); 90	88.90 (10.60); 90	0.29	(-2.89, 3.47)	0.860
EQ-5D-5L					
IMD 1	0.82 (0.22); 92	0.78 (0.22); 91			
IMD 2	0.83 (0.14); 60	0.79 (0.17); 58	0.00	(-0.05, 0.05)	0.926
IMD 3	0.87 (0.16); 79	0.82 (0.18); 79	0.02	(-0.03, 0.06)	0.489
IMD 4	0.85 (0.15); 89	0.79 (0.19); 88	-0.00	(-0.05, 0.04)	0.828
IMD 5	0.86 (0.17); 90	0.82 (0.16); 90	0.02	(-0.03, 0.06)	0.420
HUI-3					
IMD 1	0.80 (0.24); 92	0.76 (0.27); 84			
IMD 2	0.79 (0.18); 60	0.75 (0.25); 57	0.00	(-0.06, 0.06)	0.992
IMD 3	0.84 (0.19); 79	0.77 (0.24); 77	-0.01	(-0.06, 0.05)	0.857
IMD 4	0.81 (0.19); 89	0.76 (0.24); 84	-0.00	(-0.06, 0.05)	0.944
IMD 5	0.83 (0.16); 90	0.80 (0.19); 86	0.02	(-0.03, 0.07)	0.471
GUI					
IMD 1	0.88 (0.14); 92	0.87 (0.17); 90			
IMD 2	0.86 (0.11); 60	0.79 (0.18); 60	-0.06	(-0.11, -0.01)	0.011
IMD 3	0.90 (0.12); 79	0.84 (0.17); 78	-0.04	(-0.08, 0.00)	0.079
IMD 4	0.90 (0.11); 89	0.86 (0.18); 88	-0.02	(-0.06, 0.02)	0.422
IMD 5	0.91 (0.10); 90	0.88 (0.12); 88	-0.00	(-0.05, 0.04)	0.823

Values are mean (standard deviation); n. CI Confidence Interval

Supplementary Figure 1 – Subgroup for Trabeculectomy versus Medical management: (d) NEI-VFQ-25; (e) EQ-5D-5L; (f) HUI-3; (g) GUI. 1st quintile – most deprived, 5th quintile -least deprived



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