Caregiver Strain in Glaucoma

1 **Taking the strain? Impact of glaucoma on patient's informal caregivers**

2 McDonald, Leanne[1, 3]; Turnbull, Paula[2]; Chang, Lydia[2]; Crabb, David P.[1]

3 Author affiliation:

4 1. Optometry and Visual Science, City, University of London, London, United Kingdom.

5 2. Department of Ophthalmology, North West Anglia NHS Foundation Trust, Hinchingbrooke Hospital,

6 Huntingdon, United Kingdom.

7 3. Psychology, School of Human and Social Sciences, University of West London, London, United Kingdom.

8 **Corresponding author:**

9 Leanne McDonald, Psychology, School of Human and Social Sciences, University of West London, London,

10 United Kingdom; leanne.mcdonald@uwl.ac.uk.

11 **Conflict of interest:**

16

17 **Summary**

18 **What was known before**

19 • Chronic open angle glaucoma (COAG) can cause difficulties with activities of daily living such as driving

20 and mobility.

21 • Other chronic eye diseases, for example, age related macular degeneration lead to an increase in

22 reliance on family support networks; this is termed informal caregiving.

23 **What this study adds**

24 • The first to estimate caregiver strain in a sample of COAG caregivers using a validated instrument.

25 • Informal caregiver strain is negligible in most patients consecutively sampled from a glaucoma clinic in

26 England.

27 • ICG strain becomes inflated in patients with advanced visual field (VF) loss in COAG.

28 • ICG strain increases moderately with worsening VF's but in our sample some of this could be explained

29 by worse general health.

30 **Abstract**

31 **Purpose:** To estimate informal caregiver (ICG) strain in people from a glaucoma clinic.

32 **Methods:** Patients with glaucoma were consecutively identified from a single clinic in England for a cross-

33 sectional postal survey. The sample was deliberately enriched with a number of patients designated as

34 having advanced glaucoma (visual field [VF] mean deviation worse than -12 dB in both eyes). Patients were

35 asked to identify an ICG who recorded a Modified Caregiver Strain Index (MCSI), a validated 13 item

36 instrument scored on a scale of 0-26. Previous research has indicated mean MCSI to be >10 in Multiple

37 Sclerosis and Parkinson's disease. All participants gave a self-reported measure of general health (EQ5D).

38 **Results:** Responses from 105 patients (43% of those invited) were analysed; only 38 of the 105 named an

39 ICG. Mean (95% confidence interval [CI]) MCSI was 2.4 (1.3, 3.6) and only three ICGs recorded a MCSI > 7.

40 The percentage of patients with an ICG was much higher in patients with advanced VF loss (82%; 9/11)

41 when compared to those with non-advanced VF loss (31%; 29/94; p=0.001). Mean (standard deviation)

42 MCSI was considerably inflated in the advanced patients (5.6 [4.9] vs 1.5 [2.2] for non-advanced; p=0.040).

43 Worsening VF and poorer self-reported general health (EQ5D) of the patient were associated with

44 worsening MCSI.

45 **Conclusion:** ICG strain, as measured by MCSI, for patients with non-advanced glaucoma is negligible,

46 compared to other chronic disease. ICG strain increases moderately with worsening VFs but this could be

47 partly explained by worse general health in our sample of patients.

48

49 **Introduction**

50 Chronic Open Angle Glaucoma (COAG) can cause slow, irreversible damage to the visual field (VF). COAG,

51 like many other chronic conditions affecting older adults, does not limit lifespan but can make life more

52 challenging. For example, patients can report significant problems with activities of daily living, such as

53 driving, reading and mobility as their VF worsens [1, 2]. Such difficulties may lead to a reliance on a spouse,

54 partner, close friend or family member for support [3, 4]. A person caring for someone with a chronic or

55 disabling condition, but not in a formal capacity, can be termed an informal caregiver.

56 Informal caregiving, much like the condition that the patient is experiencing, can be a complex issue

57 incorporating physical, psychological, financial and emotional changes [5]. When these experiences are

58 negative, it is termed caregiver strain [6]. For example, informal caregivers have been shown to experience

59 exhaustion, problems with wellbeing and reduced levels of self-esteem [7]. Informal caregiver (ICG) strain is

60 most likely to affect women and those who do not have adequate social support [8, 9]. Conversely, ICGs who

61 are psychologically well adjusted, have good social support and implement proactive coping strategies are

62 less likely to suffer from caregiver strain [6]. ICGs often do not report their caregiver status to healthcare

63 professionals and as such may not receive appropriate support [10].

64 ICG strain is well studied in conditions like cancer [11] and mental illness [12] where burden of care is often

65 significant. More recently, ICG strain in long-term conditions has received attention. For example, ICG strain

66 in Parkinson's disease (PD) and Multiple Sclerosis (MS), was found to be significant when measured

67 quantitatively using a modified version of the Caregiver Strain Index (MCSI) [6]. The same may be true for

68 long-term chronic eye conditions. For example, ICG strain has recently been described in people with age-

69 related macular degeneration (AMD) especially as the condition leads to visual impairment [13, 14, 15, 16,

70 17]. Moreover, specific aspects of ICG strain for AMD like that associated with frequent treatment visits to

71 clinic have been flagged [14, 16]. There has also been an effort to assess ICG strain in paediatric glaucoma

72 patients [18, 19]. However, there has been no attempt to quantify ICG strain in adult COAG and this is the

73 main idea presented in this paper.

74 We estimate ICG strain in people in a glaucoma clinic in England. We do this with a cross-sectional study

75 using a widely used and well validated standardised instrument (MCSI) [20]. We primarily aim to compare

76 values from this index to values from other chronic conditions where ICG strain has been investigated using

77 the same measure, specifically those described in Peters et al. (2013) [6]. We test a secondary hypothesis

78 that measures of worsening VF in COAG are associated with worsening ICG strain as measured by MCSI.

79 **Materials and Methods**

80 We designed a cross-sectional study involving patients recruited from the glaucoma clinic of Hinchingbrooke

81 Hospital (part of North West Anglia NHS Foundation Trust). The study was approved by the NHS Research

82 and Ethics committee of the East of Scotland (17/ES/0044 ref number: 216487) and adhered to the tenets

83 of the Declaration of Helsinki. Patient participants were selected consecutively from an Electronic Medical

84 Record (EMR) (Medisoft, Leeds, UK) by the study coordinator (PT) and the clinic's main glaucoma consultant

85 (LC). To be eligible, patients (>40 years) had to be currently treated for a diagnosis of COAG with visual field

86 (VF) loss in at least one eye. COAG suspects and patients with ocular hypertension were excluded.

87 Participants were only included if they had no other ocular disease (except for uncomplicated cataract

88 extraction) and a corrected binocular visual acuity (VA) of better than LogMAR 0.3 (6/12) at their last clinic

89 visit. Patients were selected consecutively from the date they last attended clinic, and this had to be within

90 6 months of the data extraction. Names and addresses were recorded along with age (years) and a measure

91 of VF loss in both eyes (mean deviation; MD) from their last clinic visit as acquired using a Humphrey Field

92 Analyser (Carl Zeiss Meditec, Dublin, CA). The EMR also has a field for the number of significant non-ocular

93 co-morbidities and this number was recorded too.

94 We aimed to select a total of 250 patients representing a population of people with COAG being treated in

95 a clinic in England (see data analysis; sample size). We deliberately aimed to include 50 patients (some

96 selected non-consecutively) designated as having advanced COAG defined as MD worse than -12 dB in both

97 eyes. This measure for advanced VF loss has been widely used before in, for example, health economic

98 evaluations of COAG and coincides with a high-likelihood that the patient does not satisfy the VF component

99 for legal fitness to drive [21, 22].

100 A questionnaire pack, including a participant information document, was posted to the address of selected

101 participants. Due to the postal nature of the survey, participants were asked to complete a statement of

102 implied consent. The patient information document asked participants to identify an informal caregiver (if

103   applicable) with the following question: *'Can you identify someone who is an informal caregiver for your*

104   *glaucoma? This might be a spouse, a partner, a relative or friend who helps you with any aspect related to*

105   *your glaucoma.'*

106   The questionnaire pack included two sections printed on different coloured paper, one for the patient and

107   one for their potential informal caregiver (ICG). The patient section had demographic questions and a

108   validated instrument (EQ5D) to measure self-reported general health. EQ5D is commonly used by NICE (The

109   National Institute for Health and Care Excellence) for health economic evaluations for clinical interventions.

110   We used EQ5D-5L in which items are scored from 1 (no problems) to 5 (severe problems) on the five domains

111   of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. An EQ5D index score was

112   generated in a standard way with 1 representing full health (a score of 1 on all five items), and on the basis

113   of a so-called UK tariff (applicable to our participants), a worst health state of -0.594 [23].

114   If an ICG was identified by the patient, then they completed a separate section of the questionnaire with its

115   own consent statement; this included demographic questions, the EQ5D and MCSI questionnaires [20]. MCSI

116   has been widely used with more than 200 citations in the literature. MCSI estimates levels of ICG strain in

117   terms of financial, physical, psychological, social, and personal strain using 13 items, each of which is scored

118   'yes, regularly', 'yes, sometimes' or 'no'. Scores range from 0 ('no' on all items) to 26 ('yes, regularly' on all

119   items).

120   The questionnaire pack was sent with two stamped-addressed envelopes to ensure that responses could be

121   returned privately. A 'thank you' note/reminder was sent two weeks later to encourage responses. Data

122   from the questionnaires was double entered. Median imputation was used for any missing values. Data was

123   anonymised and stored in a secure location.

124

125   **Data analysis**

126 Our primary outcome was mean MCSI in the ICGs of the participating patients and a comparison with values

127 reported from a study by Peters et al. for ICGs for people with MS and PD [6]; these values were 11 and 12

128 respectively. We aligned our study to the one by Peters et al. because it used MCSI on large numbers of ICGs

129 for people with chronic conditions. From that study the between person standard deviation (SD) for MCSI

130 was 6 units. Therefore, a sample-size calculation for a one-sample t-test aiming to demonstrate a difference

131 of at least 2 units between mean MCSI in our data as compared to ones described in Peters et al. (power and

132 alpha set at 0.80 and 0.05 respectively) required at least 75 ICG responses. Assuming a response rate of 30%

133 (Peters et al. had 37%) meant we aimed to post 250 questionnaire packs.

134 Our secondary aims were to compare MCSI between ICGs of patients with and without advanced VF loss,

135 and then to explore the association between MCSI and worsening COAG as measured by VF loss corrected

136 for other measures such as, for example, sex, age and self-reported general health (EQ5D). Two-sample t-

137 tests (assumed unequal variances) were used to compare means and Chi-square tests were used for

138 categorical values. Associations were explored with Pearson correlation coefficients and a generalised linear

139 model to correct for covariance. A value of 0.05 was used for statistical significance. Analysis was done in

140 SPSS Statistics 23 (IBM Corp., Somers, NY) and in R (R Foundation for Statistical Computing, Vienna, Austria).

141 **Results**

142 We sent invitations to 243 patients, falling short of enriching our sample with our target of inviting 50

143 patients with advanced COAG (n=39); finding eligible patients fulfilling the advanced VF criteria with

144 preserved VA or not having other ocular pathology was problematic. One-hundred and sixteen (48%)

145 patients responded. Median (interquartile range [IQR]) time period between a questionnaire pack being

146 posted and returned was 14 (7, 25) days.

147 Mean (SD) age of the patients who responded (n=116) to the postal survey was 73 (10). Mean (SD) better

148 eye MD (BEMD) of the patients who responded was -3.7 (6.4). Nine patients returned questionnaires

149 declining to take part; two other patients were not analysed: on checking data entry of the clinical record

150 one was found not to satisfy the inclusion criteria for VA and the other had too many missing items to be

151 analysed meaningfully. This left 105 patients for data analysis.

152 Only 38 (36%) of the 105 patients analysed had an informal caregiver (ICG). These patients represent just

153 16% of the total of n=243 contacted, a value lower than we anticipated in our sample size calculations (30%)

154 perhaps reflecting that most people in glaucoma clinics do not consider their condition warrants an ICG. This

155 in itself is an important finding in relation to the conditions like PD and MS investigated by Peters et al. [6]

156 because in that study response rates were higher.

157 A participant stating that they had an ICG might be related to whether they are married or have a partner.

158 For example, in the patients with an ICG, 87% (33/38) self-reported they were married or in a committed

159 relationship as opposed to being single, divorced, widowed or separated; in contrast this proportion was

160 60% (40/67) in the patients who did not have an ICG and the difference was statistically significant (p=0.004).

161 Percentage of male participants with and without an ICG was 47% (18/38) and 55% (37/67) respectively;

162 these values were not significantly different (p=0.439)

163 Our primary outcome for the study was Mean (SD) MCSI; this was 2.4 (3.4) in the 38 ICGs who completed

164 the questionnaire (95% CI: 1.3, 3.6). This value was overwhelmingly statistically different (p<0.001, one-

165 sample t-test) from the mean value of ~11 reported in ICGs for people with MS and PD in Peters et al.

166 Moreover, nearly one-half (n=18; 47%) of our sample of ICG respondents returned a MCSI of zero (indicating

167 no ICG strain, responding negatively to all 13 items). Furthermore, only three ICGs recorded a MCSI >7, a

168 value that some studies have described as meaningful caregiver strain. Taken together these results suggest

169 ICG strain in COAG, as measured by MCSI, is negligible for most of the ICGs of glaucoma patients.

170 Mean (SD) best eye MD in patients with (n=38) and without (n=67) an ICG was -6.9 (9.1) dB and -2.1 (4.0) dB

171 respectively; these values are statistically different (p=0.004) hinting ICG strain increases with worsening VF

172 loss. Moreover, percentage of patients with an ICG was much higher in patients with advanced VF loss (82%;

173 9/11) when compared to those with non-advanced VF loss (31%; 29/94) and this difference was statistically

174 significant (p=0.001). To further highlight this effect of ICG strain being inflated in advanced COAG, Table 1

175 gives the patient participant and ICG response stratified by our measure of COAG severity. For example, ICG

176 mean (SD) MCSI was much worse when the patient had advanced VF loss (5.6 [4.9]). The three ICGs with

177 MCSI > 7 were for patients advanced VF loss too; this is noteworthy. There was no real evidence to suggest

178 that the sex and age profile, or number of co-morbidities, of the two groups of patients were different. Yet

179 patients with advanced VF loss, and their ICGs, had worse self-reported general health (EQ5D) compared to

180 the others in the clinic and their respective ICGs.

181

182   **TABLE 1**

183

184   Comparison between patients with and without advanced VF loss and their respective ICG responses. Means
185   with standard deviations (p-value for two-sample test [unequal variances]) and numbers with percentages
186   (p value for Chi-square test) are given for the measurements and categorical values respectively. (An asterisk
187   denotes statistical significance at p<0.05.)

188

	Patients (n=9) with advanced VF loss	Patients (n=29) with non-advanced loss	p-value
Patient age (years)	78 (9)	72 (7)	0.077
Patient: female	5 (56%)	15 (52%)	0.841
Better eye mean deviation dB	-21.5 (6.1)	-2.4 (3.2)	<0.001*
Worse eye mean deviation dB	-26.5 (4.9)	-6.8 (5.3)	<0.001*
Patient: EQ5D score	0.66 (0.21)	0.87(0.15)	0.018*
Patient: Number of co-morbidities	1.9 (2.8)	1.5 (1.4)	0.690
Modified Care Strain Index (MCSI)	**5.6 (4.9)**	**1.5 (2.2)**	**0.040***
Informal caregiver (ICG): number of females	5 (56%)	13 (45%)	0.573
Informal caregiver (ICG) : EQ5D score	0.77 (0.07)	0.91 (0.12)	<0.001*

189

190   Associations of measured variables with worsening MCSI in the 38 patients with ICGs are shown in Table 2.

191   Worsening VF and poorer self-reported general health (EQ5D) of the patient were highly associated with

192   worsening ICG MCSI. This analysis was exploratory because our study was not powered for this. Still, no

193   other variables had a statistically significant association with MCSI. Given the influence of patient EQ5D we

194 returned to our comparison of mean ICG MCSI between the patients with advanced (n=9) and non-

195 advanced VF loss (n=29) using a general linear model (sometimes referred to as ANCOVA). After controlling

196 for EQ5D as a covariate the difference in MCSI between the two groups still remained statistically

197 significant (p=0.035 vs p=0.001 [unadjusted with equal variances assumed]) but the effect diminished with

198 a mean (95% CI) difference in MCSI of 2.7 (0.2, 5.2) reduced from 4.1 (1.8, 6.4) (unadjusted). This analysis

199 still suggests having advanced VF loss inflates ICG strain but in our data this is partly explained by the same

200 patients having a co-varying worse self-reported general health. Of course, worse general health may or

201 may not be related to having advanced VF loss, but this cannot be untangled with our data.

202 **TABLE 2**

203

204 Pearson correlation coefficients for different measured variables against MCSI in 38 patients with ICGs. (An
205 asterisk denotes statistical significance at p<0.05.)

206

	Correlation coefficient (r)	p-value
Patient age (years)	+ 0.11	0.499
Better eye mean deviation dB	- 0.46	0.003*
Worse eye mean deviation dB	- 0.62	<0.001*
Patient: EQ5D score	- 0.53	0.001*
Patient: Number of co-morbidities	+ 0.31	0.063
Informal caregiver (ICG) : EQ5D score	- 0.26	0.113

207

208 MCSI items (questions) with the 38 ICG's responses are given in Table 3. One third of ICGs have at least

209 sometimes made changes in personal plans because of their caregiving. Other relatively more common

210 strains surrounded work adjustments and less time for other family members. MCSI items referring to

211 disturbed sleep, physical strain and a feeling of being 'overwhelmed' were completely rejected by all but a

212 few ICGs.

213 **TABLE 3**

214

215 The 13 items from the Modified Care Strain index questionnaire ranked by the frequency of responses by
216 the informal caregivers (ICGs). The top and bottom item in the table represent the item cited as the most
217 common and least common strain experienced by the ICGs respectively. The numbers are rounded whole
218 percent of the n=38 ICGS.
219

	Not at all	Sometimes	Regularly
There have been changes in personal plans because of my caregiving	66	31	3
There have been work adjustments because of my caregiving	76	16	8
Caregiving is confining/restricting	74	26	0
There have been other demands on my time (e.g. other family members need me) which I have been unable to deal with	76	24	0
It is upsetting to find the person I care for has changed so much from his/her former self	79	18	3
There have been family adjustments because of my caregiving	82	18	0
Caregiving is inconvenient	84	16	0
There have been emotional adjustments because of my caregiving	87	10	3
My caregiving is a financial strain	87	13	0
Some behaviour is upsetting (the person I care for has upsetting behaviours)	89	8	3
My sleep is disturbed by my caregiving	89	11	0

Caregiving is a physical strain	**92**	**8**	**0**
I feel completely overwhelmed by my caregiving	**92**	8	0

220

221 Some other results from our sample of participants are worth noting. Nearly all patients (98%; 103/105)

222 were Caucasian and 38% (40/105) self-reported being educated to degree level or higher. In our sample of

223 38 ICGs there were roughly equal numbers of men (n=18) and women (n=20); mean (SD) MCSI was similar

224 (p=0.606) for men (2.1[3.6]) and women (2.7 [3.4]) too.

225 **Discussion**

226 We used a cross-sectional postal survey to illicit a measure of ICG strain for glaucoma patients in a single

227 clinic in England. Patients were selected consecutively but the sample was enriched with a number of

228 patients with advanced VF loss. Only 36% of patients who responded felt they had an ICG and in these,

229 caregiver strain as measured by a standardised instrument (MCSI) was negligible. Although, in a subset of

230 patients with advanced VF loss in both eyes, but preserved VA and no other ocular comorbidity, the ICGs

231 response on MCSI was considerably inflated.

232 Results from this study represent new knowledge about ICG strain in glaucoma patients. Our data might be

233 useful for clinicians and practitioners who may not have considered ICG in COAG before. A raised awareness

234 is useful because there is evidence that ICGs who are given adequate support do not experience as much

235 strain [10]. Moreover, our data might be useful for targeting patients who need extra support and also health

236 economic models for glaucoma care [24].

237 Comparing MCSI values between different conditions seems attractive but is fraught with issues because of

238 the different sampling and methodology used in different studies. For example, MCSI (not the modified

239 version) >7 has been reported in 36% of ICGs of people recovering from hip fracture surgery [25], 15% of

240 ICGs of people with adult cancer [26] and 24% of ICGs of people with mild relapsing-remitting MS [27]. In

241 contrast we only had three ICGs with MCSI >7; this could be reported as 3/105 (3%) of people who were

242 contacted/replied, or 3/38 (8%) of ICGs analysed or 3/9 (33%) of the people with advanced COAG; these

243 different figures illustrate how sampling can affect results. We aligned our results to Peters et al. [6] but even

244 their study had different methodology to ours. Still, for our primary outcome, mean MCSI for ICGs of patients

245 in glaucoma clinics was considerably lower than values estimated by Peters et al. for MS and PD.

246 Greater ICG strain being related to worse VFs is another novel finding of our study; the association was true

247 in the least and most affected eye. Mean MCSI was three times larger in our sample of patients with

248   advanced VF loss compared to other patients in the clinic; this co-varied by the patients self-reported general

249   health (EQ5D) but the effect remained after statistically correcting for this. This result is unsurprising because

250   studies have indicated a rapid decline in vision related quality of life in COAG as both eyes progress to end

251   stage VF loss [28, 29] and this likely reflects the greater help these people need. Of course, our findings add

252   to the evidence that halting VF progression is a clinical imperative, not just for the patient but also for the

253   wellbeing of the ICG of a patient. A longitudinal study would be needed to explore how ICG strain increases

254   as COAG progresses in an individual and this could untangle the effect from worsening of general health.

255   ICG strain in another age-related eye condition, AMD, has been explored but making comparison with these

256   studies is also tricky. For example, a study specifically assessed people on ranibizumab (injection) therapy

257   for neovascular AMD and found it was associated with significant ICG strain [14]. Other studies have

258   highlighted ICG strain in AMD but none sampled consecutively from people in clinics nor used MCSI, so it is

259   difficult to make comparisons [13, 15]. A large multicentre cross-sectional study conducted in Portugal

260   demonstrated visual impairment, defined as worse than 0.30 logMAR (6/12) in the better seeing eye, incurs

261   ICG strain [30]. Our results from patients with advanced VF loss add to this knowledge because they had

262   inflated ICG but, because of our study design, their VA was better than 6/12.

263   There are good explanations for why ICG strain was insignificant in the majority of our sample of patients.

264   Many of these patients are receiving treatment for a condition that is almost always asymptomatic until

265   advanced in nature. In addition, patients had relatively preserved VA and no other ocular morbidity. In

266   addition, although MCSI is widely used it is unlikely to capture specific ICG strain for people with COAG. For

267   example, it was obvious that some MCSI items (Table 3), like care being physically draining, were rejected.

268   Analogous to this issue is the debate about items within patient reported outcome measures (PROMs) that

269   are not glaucoma specific and how they might, for example, be insensitive to glaucoma progression [31, 32].

270   Investigating the specific aspects of ICG strain in COAG, with a view to the development of a condition

271   specific measure would be a useful area for future work.

272 We speculate there may be ICG strain in COAG around the different treatments (drops/surgery) and this

273 could be the subject of future work. Other idiosyncratic ICG strains for COAG might include the psychological

274 burden of having a potentially blinding condition or loss of visual function that might restrict mobility or

275 remove a driving licence. We know patients are very concerned about the latter [33] and this would likely

276 impact on their ICG too. Qualitative analysis of interviews with patients and their ICGs could pinpoint these

277 strains; this is a subject of further work by our lab. In turn, this research could lead to development of a

278 simple COAG specific instrument that could be administered in a clinic to detect if there was a 'silent'

279 developing ICG strain. Others have discussed the importance of identifying a *precipice* when patients lose

280 self-medicating capability, and this might be identifiable with an appropriate instrument for the ICG [34].

281 Other results from our study are worth discussing. Any postal survey will suffer from non-response. Our main

282 findings are likely unaffected by this but ICG strain could be a little worse if everyone in the clinic was

283 captured given the association of MCSI with disease severity. The high number of patients who declared not

284 to have an ICG is interesting too. This might suggest that patients do not consider their COAG warrants an

285 ICG. Yet we also found a strong link between having an ICG and being married or having a partner. In turn

286 this highlights the importance of identifying patients who may be socially isolated or living on their own.

287 Moreover, in our data we did not observe differences in the sex profile of the ICGs, with men and women

288 reporting the same level of ICG strain. This contradicts studies where ICG strain has been thought to be

289 something that affects women more than men [8, 9].

290 Our study had several strengths. We took advantage of a widely used, standardised instrument. In addition,

291 our sampling was performed consecutively, and we measured other variables allowing for an analysis that

292 corrected for covariates. At the same time our study has several limitations. We only sampled people from

293 one centre; the patients were nearly all Caucasian and education levels were relatively high. (Some studies

294 have indicated that there may be cultural and ethnic differences in the experience of ICG strain [35].) VF

295 records were extracted from an EMR and, although unlikely, may have changed in the maximum six-month

296   period before a participant responded. Moreover, our study was only cross-sectional, relied on self-report

297   and could only examine associations. Furthermore, a larger sample and conducting he study across more

298   centres would have improved the generalisability of our results.

299   In conclusion, our study is novel in assessing ICG strain in patients from a glaucoma clinic. We conclude that

300   ICG strain in the great majority of these patients is largely negligible but, importantly, it worsens as disease

301   severity worsen. Patients with advanced VF loss in both eyes have considerably inflated ICG strain although

302   some of this might be explained by worsening general health in these people too. Further work should be

303   done to improve our understanding of the specific nuances of ICG in relation to COAG.

References

[1] Crabb D P. A view on glaucoma - are we seeing it clearly? *Eye (Lond)* 2016; **30(2)**: 304-313.

[2] Glen F C, Crabb D P. Living with glaucoma: a qualitative study of functional implications and patients' coping behaviours. *BMC Ophthalmology* 2015*;* **15:** 128.

[3] Shtein R M, Newman-Casey P A, Herndon L, Coleman A L, Lee P P. Assessing the Role of the Family/Support System Perspective in Patients With Glaucoma. *J Glaucoma* 2016: e676-e680.

[4] Keeffe J E, Chou S L, Lamoureux E L. The Cost of Care for People With Impaired Vision in Australia. *Arch Ophthalmol* 2009; **127(10)**: 1377-1381.

[5] Burleson Sullivan A, Miller D. Who is taking care of the caregiver? J Patient Exp 2015; 2(1): 7-12.

[6] Peters M, Jenkinson C, Doll H, Playford D, Fitzpatrick R. Carer quality of life and experiences of health services: a cross-sectional survey across three neurological conditions. Health Quality Life Outcomes 2013; 11: 103.

[7] van den Heuvel E, de Witte L, Schure L, Sanderman R, Meyboom-de Jong B. Risk-factors for burn-out in caregivers for stroke patients, and possibilities for intevention. Clin Rehabil 2001; 40(2): 669-667.

[8] Yee J, Schulz R. Gender differences in psychiatric morbidity among family caregivers: a review and analysis. Gerontologist 2000; 36: 147-164.

[9] McCullagh E, Brigstocke G, Donaldson N, Kalra, L. Determinants of caregiving burden and quality of life in caregivers of stroke patients. Stroke 2005; 36: 2181-2186.

[10] Royal College of General Practitioners and Royal College of Nursing. Matters of life and death: helping people to live well until they die [Internet]. London: Royal College of General Practitioners and Royal College of Nursing; 2012. Available from: http://www.rcgp.org.uk/clinical-and-

research/toolkits/~/media/Files/CIRC/Matters%20of%20Life%20and%20Death%20FINAL.ashx. [Accessed December 2016].

[11] Northouse L L, Katapodi M C, Schafenecker A M, Weiss D. The Impact of Caregiving on the Psychological Well-Being of Family Caregivers and Cancer Patients. Semin Oncol Nurs 2012; 28(4): 236-245.

[12] Chang S, Zhang Y, Jeyagurunathan A, Lau YW, Sagayadevan V, Chong S A, Subramaniam M. Providing care to relatives with mental illness: reactions and distress among primary informal caregivers. BMC Psychiatry 2016; 16: 80.

[13] Schmier J K, Halpern M T, Covert D, Delgado J, Sharma S. Impact of visual impairment on use of caregiving by individuals with Age-Related Macular Degeneraton. *Retina* 2006; **26(9)**: 1056-1062.

[14] Gohil R, Crosby-Nwaobi R, Forbes A, Burton B, Hykin P, Sivaprasad, S. Caregiver burden in patients recieving Ranibizumab therapy for neovascular macular degeneration. *PLOS One* 2015; **10(6):** e0129361.

[15] Vukicevic M, Heraghty J, Cummins R, Gopinath B, Mitchell P. Caregiver perceptions about the impact of caring for patients with wet age-related macular degeneration. *Eye (Lond)* 2016; **30(3):** 413-421.

[16] Hanemoto T, Hikichi Y, Kikuci N, Kozawa T. The impact of different anti-vascular endothelial growth factor treatment regimens on reducing burden for caregivers and patients with wet age-related macular degeneration in a single-center real-world Japanese setting. *PLOS One* 2017; **12(12):** e0189035.

[17] Gopinath B, Craig A, Kifley A, Liew G, Bloffwitch J, van Vu, J, Joachim N *et al.* Implementing a multi-modal support service model for the family caregivers of persons with age-related macular degeneration: a study protocol for a randomised controlled trial. *BMJ Open* 2017; **7(8):** e018204.

[18] Gothwal K, Bharani S, Mandal S K. Glaucoma Quality of Life of Caregivers of Children With Congenital Glaucoma : Development and Validation of a Novel Questionnaire (CarCGQoL). *Invest Ophthalmol Vis Sci* 2015; 56(1): **770-777**.

[19] Kantipuly A, Pillai M R, Shroff S, Khatiwala R, Raman G V, Krishnadas S R, Lee Robin A *et al.* Caregiver Burden in Primary Congenital Glaucoma. *Am J Ophthalmol* 2019. e-pub ahead of print: 05 July 2019: doi: 10.1016/j.ajo.2019.05.003

[20] Thornton M, Travis S S. Analysis of the reliability of the modified caregiver strain index. *J Gerontol B Psychol Sci Soc Sci* 2003; **58(2):** S127-S13.

[21] Boodhna T, Crabb D P. More frequent, more costly? Health economic modelling aspects of monitoring glaucoma patients in England. *BMC Health Serv Res* 2016; **16(1):** 611.

[22] Saunders L J, Russell R A, Crabb D P. Practical landmarks for visual field disability in glaucoma. *Br J Ophthalmol* 2012*;* **96(9):** 1185-1189.

[23] van Hout B, Janssen M F. Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health* 2012; **15(5):** 708-715.

[24] van den Burg B, Al M, van Exel J, Koopmanschap M, Brouwer W. Economic valuation of informal care: conjoint analysis applied in a heterogeneous population of informal caregivers. *Value Health* 2008; **11(7):** 1041-1050.

[25] Ariza-Vega P, Ortiz-Pina M, Kristensen M T, Castellote-Caballero Y, Jimenez-Moleon J J. High perceived caregiver burden for relatives of patients following hip fracture surgery. *Disabil Rehabil* 2019; **41(3):** 311-318.

[26] Hsu T, Loscalzo M, Ramani R, Forman S, Popplewell L, Clark K, Katheria V *et al.* Are Disagreements in Caregiver and Patient Assessment of Patient Health Associated with Increased Caregiver Burden in Caregivers of Older Adults with Cancer? *Oncologist* 2017; **22(11):** 1383-1391.

[27] van der Hiele K, van Gorp D A M, Heerings M A P, Jongen P, van der Klink J J L, Frequin S T F M, van Geel B M. Caregiver strain among life partners of persons with mild disability due to relapsing-remitting multiple sclerosis. *Mult Scler Rel Dis* 2019; **31:** 5-11.

[28] Peters D, Heijl A, Brenner L, Bengtsson B. Visual impairment and vision related quality of life in the early manigest glaucoma trial after 20 years of follow up," *Acta Ophthalmol Scand* 2015; 93(8): 745-752.

[29] Jones L, Bryan, S R, Crabb D P. Gradually Then Suddenly? Decline in Vision-Related Quality of Life as Glaucoma Worsens. *J Opthalmol* 2017; **2017**: 7 pages. Doi: https://doi.org/10.1155/2017/1621640

[30] Marques A P, Macedo A F, Hernandez-Moreno L, Ramos P L, Butt T, Rubin G, Santana R *et al.* The use of informal care by people with vision impairment. *PLOS One* 2018; **13(6):** e0198631.

[31] Skalicky S E, Lamoureux E L, Crabb D P, Ramulu P Y. Patient-reported Outcomes, Functional Assessment, and Utility Values in Glaucoma.," *J Glaucoma* 2019; **28(2):** 89-96.

[32] Jones L, Garway-Heath D F, Azuara-Blanco A, Crabb D P, UKGTS Investigators. Are Patient Self-Reported Outcome Measures Sensitive Enough to Be Used as End Points in Clinical Trials?: Evidence from the United Kingdom Glaucoma Treatment Study. *Ophthalmology* 2019; **126(5):** 682-689.

[33] Bhargava J S, Bhan-Bhargava A, Foss A J, King A J. Views of glaucoma patients on provision of follow-up care; an assessment of patient preferences by conjoint analysis. *Br J Ophthalmol* 2008; **92(12):** 1601-1605.

[34] Read S, Waterman H, Morgan J E, Harper R A, Spencer A F, Stanford P. Glaucoma, dementia, and the "precipice of care": transitions between states of medication adherence. *Patient Prefer Adherence* 2018; **12:** 1315-1325.

[35] Haley W E, Roth D L, Howard G, Safford M M. Caregiving Strain and Estimated Risk for Stroke and Coronary Heart Disease Among Spouse Caregivers. Differential Effects by Race and Sex. *Stroke* 2010; **41(1):** 331-336.