Acceptance, Attitudes, and Beliefs of Singaporean Chinese Toward an Ocular Implant for Glaucoma Drug Delivery

Reuben Chao Ming Foo,[1] *Ecosse L. Lamoureux,*[2,3] *Ryan C. K. Wong,*[4] *Sue-Wei Ho,*[3] *Peggy P. C. Chiang,*[3] *Gwyneth Rees,*[2] *Tin Aung,*[1,3,4] *and Tina T. Wong* [1,3,4]

Purpose. We investigated patients' attitudes and perceptions toward a subconjunctival implant as a novel ocular drug delivery method for glaucoma.

Methods. We recruited 344 Chinese patients with primary open angle or angle closure glaucoma currently on topical antiglaucoma medication for a minimum of six months from specialist glaucoma clinics. Sociodemographic data, and information about patients' general and ocular health were collected. Beliefs about medicines, glaucoma, eye drops, and self-reported adherence were assessed by trained interviewers using validated questionnaires. A description about the implant was provided and patients subsequently were assessed on their understanding and acceptance.

Results. Of the 344 Chinese patients enrolled, 216 (62.8%) would accept the implant as a replacement for their current eye drops. Of those who accepted the implant, 99 (45.8%) were willing to accept it at similar costs, while 40 (18.5%) and 20 (9.3%) patients were willing to pay 1.5 and 2 times the cost of their present medication, respectively. Patients who accepted the implant had more severe glaucoma ($P = 0.015$) and felt that the implant was more helpful than eye drops ($P < 0.001$). Beliefs toward medicines, glaucoma, eye drops, self-reported adherence, and sociodemographic factors did not have a significant impact on the patients' decisions.

Conclusions. An ocular drug implant would be an acceptable alternative to topical eye drops for subgroups of glaucoma patients. (*Invest Ophthalmol Vis Sci.* 2012;53:8240–8245) DOI:10.1167/iovs.12-10393

Glaucoma, affecting approximately 60 million people worldwide, is the leading cause of irreversible blindness.[1] Reduction of intraocular pressure (IOP) remains the main modifiable risk factor for the disease and the majority of patients with glaucoma are managed initially by medical treatment,[2] consisting of topical eye drops. Proportional reduction of IOP by 20% to 50% can decrease the average rate of progressive visual field loss by half.[3] Good adherence to treatment reduces disease progression in approximately 90% of cases,[4] even in normal tension glaucoma.[5]

Nonadherence to topical glaucoma medications, however, remains a problem, with up to 59% of patients reporting nonadherence to their eye drops.[6,7] Such nonadherence may be picked up only late in the disease course, due to the absence of symptoms until profound damage to the optic nerve. Studies have shown that adherence to eye drop treatment of glaucoma is similar to pill-based treatment of other chronic, asymptomatic diseases, and is less than ideal,[8] with multiple risk factors for nonadherence identified, including sociodemographic, clinical, and psychosocial factors.[9]

There is increasing global recognition of the challenges faced in optimal drug delivery for glaucoma management. A review of the current literature revealed various novel drug delivery systems being developed, including liposomes[10–12] and nanocapsules,[13] molecularly imprinted contact lenses,[14] microelectrochemical system (MEMS) drug pumps,[15] and subconjunctival injectable implants.[16] All of these aim to improve therapeutic efficiency of drugs delivered to the eye and reduce reliance on patient compliance.

Specific to subconjunctival implants for sustained drug release, Natarajan et al. recently developed a formulation of latanoprost-loaded egg-phosphatidylcholine liposomes for injection into rabbit eyes,[17] and showed that a single injection had an IOP-lowering effect comparable to daily eye drop administration without toxicity or inflammation up to 50 days.[18] To our knowledge, there has yet to be any published trials reporting therapeutic efficiency of such delivery systems in humans.

As such, there are even fewer reports evaluating the perceptions of patients toward such novel drug delivery systems, and ultimately their acceptance. Only two studies, by Dankert et al.[19] and Irani et al.,[20] have assessed psychiatric patients' attitudes toward long-term subdermal implants of psychoactive medications. In light of this unmet need and the growing interest in the field of ocular drug delivery, our study aimed to examine patients' receptiveness toward and perceptions of a subconjunctival injectable ocular implant for glaucoma drug delivery, and to determine the characteristics of subgroups of patients who are willing to accept this new technology.

Materials and Methods

Study Design

Our study was a cross-sectional study of patients receiving ophthalmic care at the Singapore National Eye Centre, a tertiary public healthcare

From the [1]Singapore National Eye Centre, Singapore; the [2]Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Melbourne, Australia; the [3]Singapore Eye Research Institute, Singapore; and the [4]Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

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Corresponding author: Tina T. Wong, Singapore National Eye Centre, 11 Third Hospital Avenue, Singapore 168751, Republic of Singapore; tina.wong.t.l@snec.com.sg.

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referral center for eye care in Singapore. Consecutive patients were screened by our research assistants from the specialist glaucoma clinics over a period of 5 months and, upon providing written informed consent, were recruited into our study. The questionnaires were translated into Mandarin and back translated into English by trained interpreters before distribution and administration between February and June 2011. The interview was conducted by a doctor at the Singapore National Eye Centre and explanation of the procedure was done via a script. Participants were interviewed in a clinic setting and were given the opportunity to clarify questions about the implant. Complex questions that could not be answered immediately by the interviewer were taken down and subsequently followed up by the principal investigator. Ethical approval was obtained from the Centralised Institutional Review Board (CIRB) of the hospital, and the study was conducted in accordance with the Declaration of Helsinki.

Participant Inclusion and Exclusion Criteria

Eligibility for our study required all participants to be diagnosed with primary open angle glaucoma (POAG) or primary closed angle glaucoma (PACG), presently on one or more topical glaucoma eye drops for at least 6 months, aged 21 years and above, of Chinese ethnicity, able to converse in English or Mandarin, and of adequate hearing to undertake the interview.

We excluded patients with a history of dry eye syndrome or ocular trauma; who were receiving current treatment with anti-inflammatory eye drops, such as steroids or non-steroidal anti-inflammatory eye drops; who had undergone an eye operation within the last three months; or who had been prescribed topical antibiotics within the last two weeks.

Measures

Baseline sociodemographic data and information about participants' general health were obtained by self report. These included age, sex, highest completed education level, monthly income, number of other medical problems, and number of non-glaucoma medications.

Information about participants' ocular health was obtained from their medical records. This included type of glaucoma, unilaterality of glaucoma, duration of glaucoma since diagnosis, severity of glaucoma in the worse eye, previous surgical treatment, and previous laser treatment. Severity of glaucoma was defined as the mean deviation (MD) of the participants' most recent reliable Humphrey visual field test, in line with the Glaucoma Staging System (GSS) by Mills et al.[21]: Stage 0: Ocular hypertension/earliest glaucoma (MD > 0.00); Stage 1: Early glaucoma (MD −0.00 to −6.00); Stage 2: Moderate glaucoma (MD −6.01 to −12.00); Stage 3: Severe glaucoma (MD −12.01 to −20.00); Stage 4: Advanced glaucoma (MD −20.01 or worse), and Stage 5: End stage (No visual field in the eye). The Humphrey visual field tests were conducted with a Humphrey Visual Field Analyzer II (Carl Zeiss Meditec, Inc., Dublin, CA) set for the central 24-2 threshold test, size III white stimulus, and SITA standard strategy. Reliability criteria for the test were taken to be less than 20% fixation losses, less than 33% false-negative errors, and less than 33% false-positive errors.

Questions that explored participants' medication regimen at the point of the study included the number of different types of glaucoma eye drops and daily dosing frequency (based on the maximum number of times eye drops were instilled each day). Combination eye drops were counted as a single type of eye drop in our analysis.

In addition, five questionnaires were administered, of which three assessed participants' beliefs: (1) Beliefs about Medicines Questionnaire (BMQ)[22] General and (2) Specific; (3) a Brief Illness Perception Questionnaire (BIPQ)[23]; (4) the Modified 8-item Medication Adherence Scale (MMAS), which assessed self-reported adherence[24]; and (5) Information about the New Procedure, which assessed understanding of the procedure.

BMQ Questionnaire.[22] The BMQ comprises two sections: the BMQ General, which assesses beliefs about medicines in general, and the BMQ Specific, which assesses beliefs about glaucoma eye drops**.**

BMQ General. The BMQ General comprises three 4-item subscales. The General-Harm Scale assesses the patients' beliefs about medicines as intrinsically harmful, addictive poisons that should not be used for long periods of time. The General-Overuse scale assesses the patients' beliefs about the way in which medicines are used and whether they are being over-prescribed by doctors who place too much trust in these medicines. The General-Benefits scale assesses the patients' beliefs about potential benefits of medicines.

BMQ Specific. The BMQ Specific comprises 13 items categorized into two subscales. The 8-item Specific-Necessity Scale assesses the patients' beliefs about the necessity of glaucoma eye drops. The 5-item Specific-Concerns Scale assesses the patients' concerns about potential adverse consequences of glaucoma eye drop usage. The BMQ Specific was developed for assessing beliefs of different medications for different illnesses.[25] In our case it was adapted to assess patients' beliefs about glaucoma eye drops on the basis of previous work.[26]

For both questionnaires, items were rated on a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). Scores obtained for the individual items in each scale were summed and averaged to give a scale score, with higher scores representing stronger beliefs in that particular scale.

BIPQ Questionnaire.[23] This is an 8-item scale designed to measure patients' cognitive and emotional representations of their illness**.** In our case, it was reworded specifically for glaucoma.

Items were rated on a 0 to 10 linear scale and higher scores represented larger magnitudes of belief in the dimension (e.g., glaucoma will last longer), and lower scores represented smaller magnitudes of belief in the dimension (e.g., poorer understanding of glaucoma).

MMAS Scale.[24] The MMAS is a further development of the Morisky-Green Test,[27] and is a structured self-reported medication adherence measure with each item measuring a specific behavior that could lead to failure of adherence**.** The MMAS has been validated previously for adherence to medications in patients with chronic diseases.[28,29]

Response choices were yes/no for the first seven items and a 5-point Likert scale response (all the time, sometimes, a little of the time, very rarely, and never) to the last question of "How often do you have difficulty remembering to take all your glaucoma eye drops"? Patients were categorized based on their scores as those who were fully adherent (perfect score of 8) and those who had incomplete adherence (score of 7 or less).

Information about the New Procedure. Questions were included to test patients' understanding of the surgical implantation procedure. A brief description about the procedure was provided in the outline format as follows:

- We are developing a new way to provide your glaucoma medication. At the moment, your medication is given to you by your doctor in bottles of eye drops. In the new method the drug will be contained in an injectable implant.
- The implant will take the form of a gel that will deliver the medicine you need everyday for up to four months after injection and will replace daily use of eye drops.
- The injection will be performed by your doctor in the clinic. Anesthetic eye drops will be put into your eye to numb it before the injection. Antiseptic eye drops then will be put into your eye to prevent an infection.
- The implant will be injected into the conjunctiva (transparent tissue covering the white of your eyeball) by your doctor. The injection will take only a few seconds.
- Risks of the injection are minimal. You may feel some mild discomfort, temporary irritation or minor bleeding but nothing more serious than that.
- The implant can be removed at any time by the doctor if necessary.

Following that, patients were asked five questions extracted directly from the text. All questions were stated in the positive to ensure no misleading information about the surgical implantation procedure was suggested.

Outcomes

To assess patients' willingness to take up the subconjunctival implant for glaucoma drug delivery, they were asked "Would you consider getting your glaucoma medicine from an implant"? Responses to the question were "Yes" or "No." Patients also were asked "How much do you think an implant could help your glaucoma"? for which responses were rated from 0 (It is not helpful at all) to 10 (It will be extremely helpful). We also wanted to find out patients' willingness to pay for this new implant compared to their current eye drops. A table listing all the glaucoma eye drops available at the Singapore National Eye Centre pharmacy along with their prices was shown to the patients. The monthly summed cost of all their glaucoma eye drops was calculated and multiplied by four (the implant was stated to last for four months) to give a figure equivalent to the amount patients would pay for four months' worth of eye drops. They then were asked "How much are you willing to pay to replace your eye drops with an implant?," with response options of less than four months' worth of eye drops, equivalent to four months' worth of eye drops, 1.5 times of four months' worth of eye drops, and 2 or more times of four months' worth of eye drops.

Statistical Analysis

Independent *t*-tests were used to determine differences between groups on parametric continuous variables. The χ^2 tests and Fisher's exact tests, where appropriate, were used for analysis of categorical data. Rasch analysis was applied to the various subscales in the BMQ General and BMQ Specific questionnaires to determine if the summation of scores from each question provided a reliable and valid assessment of the latent traits each subscale was constructed to assess, that is the various beliefs of participants toward medicines and glaucoma eye drops. It determines the psychometric properties of the scales, such as how well items fit the underlying latent trait being measured, how well items discriminate between the respondents, how well item difficulty targets person ability, and the appropriateness of the response scale used. Winsteps (Ver. 3.72.3; Winsteps, Chicago, IL) was used to perform Rasch analysis with the Andrich rating scale model. The validity of each scale was assessed for item fit, behavior of response categories (i.e., if higher categories represented better ability), measurement precision (minimum person separation index [PSI] of 2.0 and person reliability [PR] of >0.8), unidimensionality, and targeting of items to the patient's level.[30]

Variables associated significantly with implant acceptance then were entered into a multivariate logistic regression model to identify independent predictors of implant acceptance. Significance levels were set at $P < 0.05$. All analyses were done with SPSS v17.0 for Windows (IBM, Chicago, IL).

Results

Sample Characteristics

Of 400 patients deemed eligible, 344 (86.0%) subsequently agreed to be interviewed. Study subjects were 30 to 91 years old, with a mean age of 66.1 years (SD 10.22 years). Of our patients, 223 (64.8%) were male and 314 (91.3%) of them completed at least primary level education. Mean duration of glaucoma was 4.17 years (SD 3.66 years). Our patients used an average of 1.63 (SD 0.692) eye drops at a mean dosing frequency of 1.78 times per day (SD 0.55 times per day). Severity of glaucoma (of our patients' worse eye) was measured via the MD on the Humphrey visual field test and the average score of the sample was −13.54 (SD 9.66).

Of our patients 156 (45.3%) had previously undergone some form of surgery; 82 (23.8%) bilateral versus 74 (21.5%) unilateral. Stratifying by types of surgery, 83 (24.1%) had phacoemulsification only, 35 (10.2%) had trabeculectomy only, 59 (17.2%) had phacoemulsification with trabeculectomy, 12 (3.5%) had extracapsular cataract extraction, and 7 (2.0%) had other surgery. A total of 107 (31.1%) patients had undergone some form of laser treatment for their eyes; 77 (22.4%) bilateral versus 30 (8.7%) unilateral. Stratifying by types of laser procedures, 81 (23.5%) had peripheral iridotomy, 18 (5.2%) had trans-scleral cyclophotocoagulation, and 16 (4.7%) had selective laser trabeculoplasty.

With regards to our patients' general health, 265 (77.1%) had at least one other medical problem, and they were on an average of 2.35 (SD 2.09) types of non-glaucoma medications.

Rasch Analysis

Rasch analysis was performed on the three BMQ General subscales (Harm, Overuse, and Benefits) and two BMQ Specific subscales (Necessity and Concerns) for all 344 questionnaires. The BMQ General–Benefits subscale was a poorly constructed scale and could not be rescored with Rasch analysis. It subsequently was removed. Items from each questionnaire then were fitted to the Rasch model.

There was initial evidence of disordered thresholds for all the scales. Examination of these items for the BMQ General and BMQ Specific indicated that Response 3 "Uncertain" on the 5-point Likert scale did not have a point along the ability continuum where it was the most likely response. Consequently, categories were collapsed for subsequent analysis. Only item 1, "My health, at present, depends on my eye drops," from the BMQ Specific–Necessity subscale demonstrated item misfit, that is having in fit residual values >1.3. After its removal, the remaining items subsequently showed values of <1.3. The PSI was modest with scores ranging from 1.33 to 0.67. The principal component analysis (PCA) for dimensionality varied. The BMQ General–Harm subscale explained only 37.4% of the raw variance, and the unexplained variance by the first contrast of the residuals was 1.7 eigenvalues units. The BMQ Specific–Necessity subscale reported the highest raw variance of 53.9% and had a first contrast of the residuals of 1.8 eigenvalues units. The mean target values of each participant for the various subscales varied from −2.07 to 0.98 with SD ranging ± 1.40 to 2.78.

Overall the differences in item and participant means were relatively small, suggesting that participants had similar ability with the scale items and that items in both questionnaires were neither too easy nor too difficult. There was no evidence of differential item functioning among age and sex. However, in view of the modest PSI, person reliability scores, and mean target values, the BMQ instruments were deemed unable to discriminate the sample and subsequently removed from further analysis.

Differences in Patients by Acceptance of Implant

Within our sample of 344 patients, 216 (62.8%) reported that they would consider taking up the implant. Table 1 outlines the sample characteristics by patients who would and would not accept the implant. Male patients and those having completed at least primary school education were more likely to accept implants ($P < 0.05$). Patients who accepted the implant also had a shorter duration of glaucoma (3.77 vs. 4.86 years, $P = 0.010$), poorer Humphrey visual field MD scores (−14.41 vs. −12.04, $P = 0.022$), more non-glaucoma medica-

Table 1. Patients' Characteristics Stratified by Acceptance of Implant

Patient Characteristics	Acceptance of Implant ($n = 216$)	Nonacceptance of Implant ($n = 126$)	*P* Value
Age, y			
Mean (SD)	65.5 (10.0)	67.0 (10.6)	0.181
Sex			
Male*	158 (72.5%)	65 (51.6%)	<0.001
Education level			
Primary completed*	206 (94.5%)	108 (85.7%)	0.005
Personal income			
$1500/mo or less	173 (79.4%)	105 (83.3%)	0.367
Type of glaucoma			
POAG	166 (76.1%)	105 (83.3%)	0.116
Unilateral			
Yes	38 (17.4%)	26 (20.6%)	0.462
Diagnosis of glaucoma, y			
Mean (SD)*	3.77 (3.46)	4.86 (3.90)	0.010
No. of eye drops			
Mean (SD)	1.67 (0.72)	1.56 (0.63)	0.125
Dosing frequency/day			
Mean (SD)	1.79 (0.56)	1.76 (0.53)	0.557
Severity of glaucoma			
Mean (SD)*	−14.41 (10.16)	−12.04 (8.55)	0.022
Previous surgical treatment			
Yes*	90 (41.3%)	66 (52.4%)	0.046
Previous laser treatment			
Yes	73 (33.5%)	34 (27.0%)	0.209
No. of medical problems			
Mean (SD)	1.79 (1.34)	1.56 (1.20)	0.095
No. of other medications			
Mean (SD)*	2.52 (2.20)	2.04 (1.86)	0.034

* Significant at 0.05 level.

tions (2.52 vs. 2.04, $P = 0.034$), and no previous surgical treatment ($P = 0.046$). Stratification of previous surgical and laser interventions by type made no difference to the outcome of implant acceptance.

Differences in beliefs of patients by implant acceptance are reported in Table 2. Patients more concerned about their glaucoma ($P = 0.011$) were more likely to accept the implant. With regards to perceptions of implant helpfulness, patients who would accept the implant scored it more highly than those who would not (6.78 vs. 4.55, $P < 0.001$). There were, however, no significant differences between groups in their other beliefs or their adherence (all $P > 0.05$).

Our study also assessed patients' understanding of the surgical implant procedure and we found our sample's average accuracy to be 95.7%. We also found that there were significant differences in scores for a single question concerning whether medicine would be released by the implant for many months, with patients correctly answering the question being more likely to take up the implant ($P < 0.001$). Overall, patients were more likely to take up the implant if they answered all 5 questions correctly ($P = 0.001$).

Table 3 shows the breakdown of the amount patients reported to be willing to pay for the implant by acceptance. The majority of patients in both groups were willing to pay the same amount (45.8% and 50.0%, respectively) compared to their current eye drops. Intuitively, more patients among those who accepted the implant were willing to pay more (27.8% vs. 18.2%), while more patients among those who rejected the implant preferred the costs to be lower than that of their current eye drops (31.7% vs. 27.3%).

Table 2. Results of Patient Beliefs by Acceptance of Implant

Belief Measures	Mean (SD)/*N* (%) Acceptance of Implant ($n = 218$)	Mean (SD)/*N* (%) Nonacceptance of Implant ($n = 126$)	*P* Value
BIPQ			
Consequences	4.62 (3.01)	4.02 (3.19)	0.078
Time line	8.14 (2.44)	7.67 (2.67)	0.111
Personal control	5.56 (2.61)	5.50 (2.90)	0.833
Treatment control	6.82 (2.30)	6.74 (2.43)	0.765
Identity	3.36 (2.65)	2.89 (2.78)	0.118
Concerns*	7.82 (2.87)	6.90 (3.37)	0.011
Illness coherence	4.92 (3.23)	5.08 (3.09)	0.658
Emotional response	3.57 (3.24)	2.98 (3.37)	0.108
MMAS			
Full adherence score of 8	68 (31.2%)	33 (26.2%)	0.326
Implant helpfulness score*	6.78 (1.97)	4.55 (2.02)	<0.001

* Significant at 0.05 level.

Multivariate Logistic Regression Analysis

Table 4 shows the results of our multivariate logistic regression analysis. Independent factors associated with implant acceptance included poor MD values on the Humphrey visual field test ($P = 0.024$) and a good perception of implant helpfulness ($P < 0.001$).

Discussion

Despite novel ocular drug delivery methods being explored globally, few studies have assessed glaucoma patients' perceptions and acceptance toward these alternative routes of administration. Subconjunctival implantation is promising because it has been shown to be safe and efficacious in animal trials,[17,18] and may revolutionize the chronic problem of poor patient adherence. Patient acceptance, therefore, is a crucial component for its implementation. Our study compared preferences between eye drops and an injectable implant of Singaporean Chinese patients, and found that with an implant acceptance rate of 62.8%, patients may be receptive toward this new method of sustained delivery.

Cost has been identified as a factor affecting adherence toward glaucoma treatment regimens,[9] thus it also may be a factor affecting acceptance of the implant. We looked at our patients' willingness to pay toward this new drug delivery method, and found that almost half and one-quarter of them were willing to pay an amount equivalent to or above the costs of their current treatment, respectively. Our patients on topical glaucoma medications preferentially opted for an alternative and cost did not appear to be a limiting factor. This is in line with the study by Jampel et al., which reported that 50% and 69% of patients would choose a larger copayment of an eye drop if it required fewer instillations, down from thrice daily to twice and once daily instillation, respectively.[31]

Of the 344 patients surveyed, an overwhelming majority of 243 (70.6%) patients reported incomplete adherence to their glaucoma medications. Tsai et al. classified barriers to adherence into four specific categories of regional, patient-related, provider-related, and environmental factors.[26] A 4-

Table 3. Cost of Implant Acceptable to Patients by Acceptance of Implant

Response	Acceptance of Implant ($n = 216$)	Nonacceptance of Implant ($n = 126$)
Less than 4 mo worth of eye drops	59 (27.3%)	40 (31.7%)
Equivalent to 4 mo worth of eye drops	99 (45.8%)	63 (50.0%)
1.5 times 4 mo worth of eye drops	40 (18.5%)	13 (10.3%)
2 or more times 4 mo worth of eye drops	20 (9.3%)	10 (7.9%)

monthly subconjunctival injection would reduce some of these barriers. We suggested that such an alternative may be useful for optimizing treatment in our patients.

Previous studies investigating attitudes and beliefs of patients toward chronic illnesses, such as asthma, systemic lupus erythematosus, and cardiac and renal disease, reported that patients' beliefs were more powerful factors than clinical factors in affecting medication adherence and subsequent treatment outcome.[25,32,33] Our findings, in contrast, showed that although subjective beliefs toward glaucoma, medicines in general and eye drops were associated with acceptance of ocular implants, they were not independent predictors in multivariate analysis. The subgroups of patients who were more likely to take up the implant were those who had severe glaucoma and those who perceived the implant to be helpful. We defined "helpfulness" as an overall improvement and convenience in the management of glaucoma, not in terms of adherence or the lowering of the IOP.

We hypothesized that this difference could be due to the aforementioned chronic illnesses differing from glaucoma in terms of their disease progression. By having characteristic well-defined episodes of symptomatic manifestations, for example asthma exacerbations, lupus flares, myocardial infarctions, and acute fluid overload states, these patients receive "feedback" and are influenced to have stronger beliefs, which in turn affect their adherence and treatment outcome. Glaucoma, also known as the silent thief of sight, affects mostly peripheral vision and remains asymptomatic until the later stages in the disease. Therefore, individuals with severe glaucoma were more likely to accept the implant because they experienced more visual symptoms, uncontrolled by eye drops, compared to subjects who had milder disease. Further studies are needed to confirm our hypothesis.

Health literacy is important for optimizing patient education and improving clinical outcomes.[34] Despite our best efforts to ensure patients' understanding of the questions in our study, we acknowledge that some patients may not have fully comprehended the concept of a subconjunctival injection as health literacy was not assessed formally. However, our interviewer-administered script provided simple explanations for medical terms, such as "conjunctiva" – "the transparent tissue covering the white of your eyeball," "anesthetic eye drops" – "to numb your eye," and "antiseptic eye drops" – "to prevent an infection," to ensure patients would not be confused by medical jargon. For the majority of our patients (91.3%) who completed at least primary school education, Rasch analysis of our questionnaires showed that the questions included were neither too easy nor too difficult.

With regards to measuring adherence, we used the self-reported MMAS, which was simple, practical, and efficient in its administration, as it gave us a patient's perspective of their adherence. This questionnaire was ideal as we did not set out to find out the association between true adherence, that is an exact measure of when and how patients took their medications, and implant acceptance. Instead, we were more interested in patients' perceptions of their own relative standing on the adherence dimension. These self-report measures also have been shown to be accurate and to provide useful qualitative information about medication adherence.[35,36]

However, one should keep in mind the following limitations while interpreting the results of our study. We did not explore directly the reasons behind patients' acceptance of the implant and, hence, were only able to hypothesize reasons for acceptance or rejection based on the associations found. Also, due to the constraints of a busy clinic, we were unable assess our patients' abilities to instill eye drops properly. Difficulty in eye drop instillation by a patient could be a strong reason for implant acceptance. These are important issues that future studies should address, along with the perceptions of patients' family members' toward such an implant.

The multiple negative outcomes of nonadherence[37] have driven research to develop patient-independent sustained drug delivery methods. Our findings affirm the value of a subconjunctival injection as an acceptable alternative to topical eye drops in the Chinese population in Singapore, in particular those with severe disease, and we hope that our work will facilitate future research into other novel drug delivery-optimizing therapies.

Table 4. Summary of Multivariate Logistic Regression Analysis

Variable	Odds Ratio	95% Confidence Interval	*P* Value
Male sex	1.719	(0.962, 3.073)	0.067
Completed primary education	1.456	(0.551, 3.846)	0.448
Shorter duration since diagnosis of glaucoma	1.085	(0.999, 1.176)	0.054
More severe glaucoma*	1.040	(1.007, 1.073)	0.015
Previous surgical treatment	0.581	(0.316, 1.066)	0.080
Greater number of other medications	1.133	(0.989, 1.299)	0.072
Higher scores on BIPQ–Concerns scale	1.032	(0.939, 1.135)	0.515
Higher implant helpfulness score*	1.703	(1.455, 1.992)	<0.001
Answered "Information about Procedure" question 4 correctly	4.732	(0.531, 42.160)	0.164
Perfect score of 5 for "Information about Procedure"	1.089	(0.480, 2.473)	0.838

* Significant at 0.05 level.

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