

BMJ Open Responsiveness of the HUG-5 in an outpatient clinic: a 12-month randomised feasibility study protocol

Kevin Kennedy ,¹ Keanan Nanji ,² Nikhil Patil ,³ Michael Wu,³ Jim Xie,³ Jenny Chan,³ Amin Hatamnejad,³ Brian Chan,² Feng Xie ,⁴ Enitan Sogbesan²

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¹Health Research Methods, Evidence and Impact, McMaster University Faculty of Health Sciences, Hamilton, Ontario, Canada

²Department of Surgery, Division of Ophthalmology, McMaster University Faculty of Health Sciences, Hamilton, Ontario, Canada

³Michael G DeGroot School of Medicine, McMaster University, Hamilton, Ontario, Canada

⁴Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada

Correspondence to

Kevin Kennedy;
kennek12@mcmaster.ca

ABSTRACT

Introduction Glaucoma is a progressive, chronic condition that can have a significant impact on a patient's health-related quality of life (HRQoL). Validated, disease-specific HRQoL tools such as the Health Utility for Glaucoma (HUG-5) tool and the Glaucoma Quality of Life Questionnaire (GlauQoL-17) can be used to monitor a patient's quality of life. However, the utility of these tools in outpatient clinic practice is not well established. The primary objective of this study is to characterise the feasibility of administering periodic HRQoL questionnaires in glaucoma using a semi-automated workflow.

Methods and analysis This study will be a single-centre, unblinded, randomised, parallel-group study with an exploratory data analysis framework. We aim to determine the feasibility of administering the HUG-5 in an outpatient clinic using a semi-automated workflow and determine patient engagement through email and telephone contact methods. We will also be investigating the association of the HUG-5 and GlauQoL-17 with patient visual field testing and visual acuity. Mean differences between groups will be tested with analysis of variance to determine if the frequency of calls affects burden, satisfaction and perceived value of information.

Ethics and dissemination This study has been approved by the Hamilton Integrated Research Ethics board (ID: 13046) and will be conducted within Canadian Tri-Council Statement policy. Personal information of the study's participants will be anonymised with identification codes and data will be kept on an encrypted server. Results of this study will be disseminated through peer-reviewed journals, conferences and internal meetings.

INTRODUCTION

Glaucoma is a clinical term that describes a group of ocular disorders with characteristic optic neuropathy and a distinct associated pattern of progressive visual dysfunction.¹ Glaucoma progression and treatment are not associated with mortality,² but have significant effects on a patient's health-related quality of life (HRQoL).³ HRQoL is a multifactorial concept representing a patient's perception of the quality of their physical, mental and social dimensions of life.⁴ For patients with glaucoma, decisions regarding treatment play

Strengths and limitations of this study

- We will collect data over intervals which mimic real life intervals for glaucoma follow-up visits and will match the health-related quality of life information with clinical outcomes.
- We will assess how patients in this demographic engage through a semi-automated email workflow versus through phone.
- Inclusion of patients with only mild–moderate glaucoma is not representative of the overall glaucoma population.
- The 60-day buffer between visual field test results and visual acuity measurements to the initial completion of the Health Utility for Glaucoma-5 and Glaucoma Quality of Life Questionnaire-17 limit conclusions of relationships described.

a significant role in their HRQoL.^{3,4} There is significant variability in how patients report experiencing their disease and treatment. Therefore, individual patient information should be considered when deciding on a patient's management.^{3,4} Integrating patient-reported HRQoL data with clinical evaluations has been increasingly recognised as the preferred approach when treating glaucoma and is the goal of therapy as per the most recent glaucoma clinical practice guidelines by the Canadian Ophthalmology Society.⁵

When evaluating HRQoL in patients with visual dysfunction, disease-specific measures are preferred given the relatively low sensitivity and responsiveness of generic HRQoL measures.⁶ The Health Utility for Glaucoma (HUG-5) and the Glaucoma Quality of Life Questionnaire (GlauQoL-36) are two disease-specific measures of HRQoL validated on samples of patients with glaucoma.^{7–9} The GlauQoL-36 is a well-established tool for assessing HRQoL in patients with glaucoma with the shorter GlauQoL-17 being used in clinical practice.⁸ The HUG-5, given its length, takes less time to administer.

There is an opportunity to integrate information pertaining to HRQoL in patient assessments between visits and to understand the impact of therapies on patient quality of life over time. This feasibility study was proposed to explore the impact of implementing routine HRQoL measures and determine how patients respond to measurement frequency. We aim to determine the feasibility of implementing these measures in practice by evaluating the response rate, call burden, satisfaction with care and value of information from patients. This information will be compared between the different call frequencies and between the two measures. We also hope to gain insight into the responsiveness of the measures by comparing the HUG-5 and GlauQoL-17 in their ability to detect changes in HRQoL over time and their relationship to changes in visual outcome parameters. This prospective study is designed as a randomised, unblinded feasibility study with three frequencies of survey administration including once every 3 months, 6 months and 12 months. Randomisation will be performed using a computerised system with a 1:1:1 allocation.

Objectives

Our primary objective will be to determine the feasibility of administering the HUG-5 in an outpatient clinic using a semi-automated workflow and determine patient engagement through email and telephone contact methods. Our secondary objective is to determine if there is an association between the HUG-5 or the GlauQoL-17 and the patient's visual field testing results or visual acuity.

METHODS AND ANALYSIS

This study will be a single-centre, unblinded, randomised, parallel-group study with an exploratory analysis framework. Below, we outline a proposed method of collecting HRQoL data, the outcomes of interest and the appropriate statistical analysis to address our primary and secondary research questions. The most recent study protocol (V.3) has been approved by the Hamilton Integrated Research Ethics board (HiREB) ethics board as of 14 September 2021. A data monitoring committee is not needed as we are not collecting adverse events, or any information associated with an obligation to report. Data quality and completion rate will be assessed every 3 months by study investigators. Should protocol amendments be made, they will be approved by the HiREB and all participants will be informed.

Inclusion criteria and recruitment

Eligible patients will have a confirmed diagnosis of mild or moderate primary open-angle glaucoma in one or both eyes. Staging will be performed according to the Canadian Ophthalmology Society glaucoma clinical practice guidelines. Specifically, a vertical cup-to-disc ratio of <0.65 and/or a visual field mean deviation of better than -6 dB will be considered mild glaucoma. A vertical cup-to-disc ratio of 0.65 – 0.90 and/or a visual field mean

deviation of -6 to -12 dB will be considered moderate glaucoma.⁵ Patients will be at least 18 years of age, have had visual field and visual acuity testing conducted within 60 days prior to completion of baseline HRQoL questionnaires and be able to speak and write English and provide consent. Patients who meet these criteria and are presently seeking care from an outpatient ophthalmology clinic in Hamilton, Ontario, Canada, will be contacted for inclusion in the investigation. Patients will be identified by their ophthalmologist through an electronic medical record search. Phone numbers, names and emails will be extracted from the patient record and stored with encryption and can only be accessed using a secure password. An investigator (NP/MW/JX) will call the patient to inquire regarding their interest in joining the study. Patients who meet the study inclusion criteria will be associated with a study schedule at random as determined by a computer-generated random value until the desired sample size is reached with appropriate allocations. Patients will also be informed of their right to withdraw from the study at any point with no consequence. Once verbal informed patient consent has been obtained, the patient will be asked if they have difficulties accessing or using email. If there are no difficulties, the patient will be contacted after 1 week via email and provided with a consent form for their records. Subsequent contacts with the patient will be by email in accordance with their prescribed schedule to record responses to study measures in the study application. If a patient identifies challenges accessing personal email, the patient will be mailed a physical copy of the consent form. After 1 week the patient will be called to be briefed on study protocol and obtain verbal consent. Future questionnaires for patients identifying their preference for contact by phone will complete the same procedures through the research assistant accessing the study application, entering the participant code and asking HRQoL questions verbally. Throughout the study period, patient responses and data quality will be monitored by study investigators. Care providers will be blinded to the patient's assignment to questionnaire frequency. In the event a patient misses a scheduled response, an investigator will follow-up with the patient by phone call if the measures are not completed within 7 days of the email being sent.

Randomisation

Patients will be randomised 1:1:1 to one of three conditions using computer-generated random numbers: (1) to complete the measures at enrolment and study completion, (2) to complete the measures every 6 months and (3) to complete the measures every 3 months. Patients will receive emails with a unique code to enter their responses over the course of 12 months at the prespecified intervals. As mentioned previously, participants will have the option of completing the questionnaire over the phone if they are unable or unwilling to do so by email. Frequencies were determined to capture three levels of information for a 12-month period: low (two measurements),

moderate (three measurements) and high (five measurements). These specific frequencies were selected as significant changes in HRQoL in patients with glaucoma have previously been detected at 6-month and 12-month intervals.³ A group with data collected at 3-month intervals will be implemented to determine if there is an added benefit to more frequent measurements.

HRQoL measures

The HUG-5 is a five-attribute, disease-specific, preference-based measure.⁷ Each attribute has five response levels and corresponds to one of five HRQoL dimensions: visual discomfort, mobility, daily life activities, emotional well-being and social activities. The HUG-5 describes a total of 3125 health states. This measure takes patients less than 2 min to complete and was developed based on information collected through a systematic literature review, patient interviews and a series of focus groups. The measure was validated on a sample of patients with various types of glaucoma, demonstrating sensitivity to distinguish between severe and moderate/mild disease states (using Hodapp-Parrish-Anderson Staging with mean deviation). The HUG-5 dimensions showed sufficient concurrent validity with quality of life subscales measured by the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) and a high degree of reliability following a 3-month measurement from a subset of respondents.¹⁰ The GlauQoL-36 is a 36-question, clinically validated tool for assessing the following seven domains: psychological well-being, self-image, daily life, driving, anxiety, burden of treatment and confidence in healthcare.⁹ This tool covers all stages of the disease from isolated ocular hypertension to advanced glaucoma, however, its completion requires high effort likely due to its length. The GlauQoL-36 is able to detect changes to a patient's quality of life without necessitating functional changes as well.^{8,9} The GlauQoL-17 is a shortened version intended for use in clinical practice and will be used in this study as we are interested in the applicability of HRQoL measures in a real-world setting.

Data collection and management

At enrolment, patients will be briefed on the nature of the study and asked to provide informed consent. If they are interested in enrolling, but unable or unwilling to complete the questionnaires through the email contact method, they will be offered the option to complete the questionnaires over the phone. Participants will receive \$C10 in the form of an electronic gift card as compensation for their involvement in this study. Following enrolment, patients will receive emails at the prespecified intervals with links to respond to the HUG-5 and GlauQoL-17.

Demographics and responses to the two HRQoL measures (HUG-5 and GlauQoL-17) will be recorded. The unique link will be associated with the study identifier in a separate, encrypted database, where patient clinical/contact information will be encrypted at rest. Clinical data

will be extracted on location by trial investigators (KN/NP/MW/JX) into Microsoft Excel (2021) before being integrated into the NoSQL database. Survey data from the HUG-5 and GlauQoL-17 will be collected through an online application and stored separately with a linked primary key to track responses over time. The duration of time spent on each measure will be recorded. All interactions with the application will be logged. This server will perform daily scheduled decryption, send automated emails and conduct re-encryption to ensure data security. The emails will contain a prompt for enrolled patients to visit the application, containing a link to the application and a unique code for access. If patients do not complete their assessment, patients will be called directly by study investigators after a period of 7 days. Calls will be scheduled at three times to accommodate patients who may be working shifts at different times. During this call, patients will be asked if they would like to go through the study questionnaires with the investigator (NP/MW/JX) or complete them on their own. At the end of this call, patients will be asked for feedback as to why they did not respond to the initial prompt to identify barriers to the implementation of this data collection method.

At the end of the 12-month period, patients will be asked to reflect on their participation in the study and indicate: the call burden associated with each measure, overall satisfaction with their care, whether they believe this information was important to share with their ophthalmologist and if this programme were to be implemented in their clinic, how frequently they would be willing to share this information. The timeline of this project is summarised in [figure 1](#). For patients who withdraw at any point in the study, a study investigator will follow-up with them to document any comments they are willing to provide regarding their decision to withdraw.

Electronic medical records

To supplement the information shared by each patient, date of birth, appointment dates, surgical history, medication history and visual field loss as measured by differences in mean deviation (-db) over the course of the 12 months will be collected. Visit frequency will be at the discretion of the treating ophthalmologist (BC). Clinical records will be extracted following the final call and stored in an encrypted, password-protected data file.

Outcomes of interest

Our primary outcome is to determine the feasibility of implementing these HRQoL measures in practice. Feasibility will be evaluated with the enrolment rate, response rate, call burden, satisfaction with care and value of information from patients. Response rate will be defined as the average rate of patients receiving calls and reporting their HRQoL. Call burden will be measured on a 1–7 Likert scale where patients rate the burden of being administered the HUG-5 and the burden of being administered the GlauQoL-17. Satisfaction with care will be measured on a 1–7 Likert scale where patients indicate

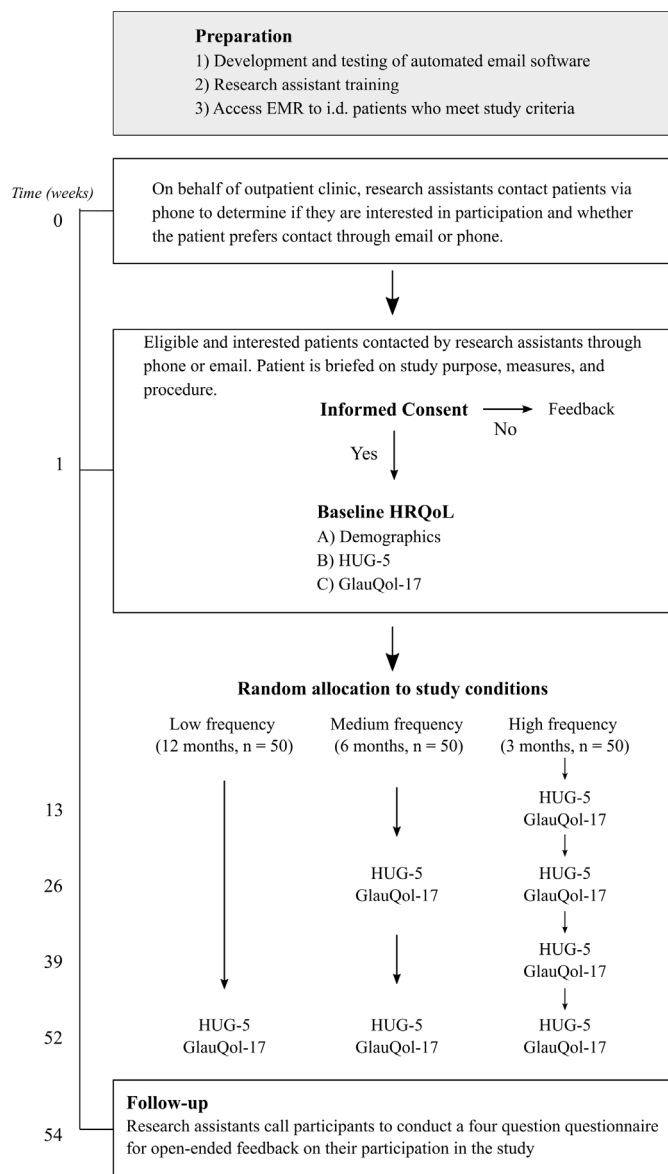


Figure 1 Study design and data collection timeline. EMR, electronic medical record; GlauQoL, Glaucoma Quality of Life Questionnaire; HRQoL, health-related quality of life; HUG, Health Utility for Glaucoma; i.d., identify.

their satisfaction with their glaucoma care. Value of information will be measured on a 1–7 Likert scale where patients rate how important they believe the information collected is for their ophthalmologist to know. These data will be compared between the different call frequencies and between the two measures.

Our secondary objective is to gain insight into the responsiveness of the measures by comparing their ability to detect changes in HRQoL over time and their relationship to changes in visual field and visual acuity testing. Longitudinal changes in patients' visual field and visual acuity loss will be applied in a linear regression with HRQoL grouped by frequency of measurement. The HUG-5 and GlauQoL-17 will be contrasted as terms in this regression (predicting visual field loss) to generate preliminary data. We aim to understand the

distribution of possible effects and sample size required for future investigations aimed at determining measurement responsiveness.

Effective sample size and statistical analysis

Provided that the primary outcome is to determine the feasibility of implementing the HRQoL measures into practice, a power calculation was not undertaken.^{11–13} A literature review was performed to help guide the optimal sample size to inform our primary outcome; no consensus was found with suggestions ranging from 12 per group to 50 per group.^{14–18} We decided to proceed with the most inclusive estimate of 50 participants per group to determine the feasibility of implementing the HRQoL measures into practice. As this is a feasibility study, no statistical methods will be used to infer values for missing data. Differences of means between groups will be tested with analysis of variance to determine if the frequency of calls affects burden, satisfaction and perceived value of information. We anticipated that we would require review of 600 patient charts with glaucoma in one or both eyes. We conservatively estimated that 50% of patients eligible would agree to receive more information at the initial recruitment call. Of the 300 patients, we expect 50% to complete enrolment, resulting in 150 patients comprising the effective sample. Analyses and calculations will be conducted in R statistical software V.4.1.1.¹⁹

Ethics and dissemination

This study has been approved by the HiREB (ID: 13046) and will be conducted within Canadian Tri-Council Statement policy. Personal information of study participants will be anonymised with identification codes and stored in a secured, encrypted server. The final data set will only be accessible to study investigators and will be deleted 5 years following publication. We plan to share the results of this study widely through peer-reviewed journals, conferences and internal meetings. We do not intend to conduct any interim analyses. All authors will adhere to the guidelines suggested by the International Committee of Medical Journal Editors Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. No professional writers will be used.

Patient and public involvement

Patients were not included in the design of this study and will not be included in the analysis.

Twitter Jenny Chan @Jenny_J_Chan and Feng Xie @fengxie_mac

Contributors KK and KN conceptualised the research goals and aim, developed methodologies and wrote original draft and were responsible for funding acquisition. NP, MW, JX, JC and AH contributed to the preparation and supported original draft for publication of the protocol, improving methodologies and further specifying research goals and aims. FX, BC and ES contributed to the preparation of the original draft of research goals and methods and reviewed this article before submitted for publication. All contributed to funding acquisition as senior investigators. All authors approved the final draft of this protocol prior to submission for publication.

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Competing interests None declared.

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ORCID iDs

Kevin Kennedy <http://orcid.org/0000-0001-8230-091X>

Kean Nanji <http://orcid.org/0000-0002-7176-6631>

Nikhil Patil <http://orcid.org/0000-0003-3929-0482>

Feng Xie <http://orcid.org/0000-0003-3454-6266>

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