A Randomised Control Trial to Compare Quality of Recovery between Desflurane and Isoflurane Inhalational Anaesthesia in Patients Receiving General Anaesthesia for Ophthalmological Surgery at a Tertiary Hospital

(DIQoR Trial)

ClinicalTrials.gov: NCT04188314

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1 Administrative Information

1.1 Trial Registration

1.1.1 Registry

Registered in ClinicalTrials.gov with reference number: NCT04188314.

Submitted protocol to National Health Research Database (NHRD) – awaiting feedback.

1.1.2 WHO Data Set

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov: NCT04188314
Date of registration in primary registry	4 December 2019
Secondary identifying numbers	SAHPRA Phase IV Notification: N20210205
Source(s) of monetary or material support	JPRF Research Fund
Primary sponsor	JPRF Research Fund
Secondary sponsor(s)	Abbvie Scholarship
Contact for public queries	C. Steyl: csteyl1@gmail.com
Contact for scientific queries	C. Steyl: csteyl1@gmail.com
Public title	Comparing Quality of Recovery Between Desflurane & Isoflurane in Eye Surgery Patients at Dr George Mukhari Academic Hospital (DIQoR Trial)
Scientific title	A Randomised Control Trial to Compare Quality of Recovery between Desflurane and Isoflurane Inhalational Anaesthesia in Patients Receiving General Anaesthesia for Ophthalmological Surgery at Dr. George Mukhari Academic Hospital (DIQoR Trial)
Countries of recruitment	South Africa
Health condition(s) or problem(s) studied	Quality of Recovery after General Anaesthesia
Intervention(s)	Control drug: Isoflurane Intervention drug: Desflurane
Key inclusion and exclusion criteria	Ages eligible for study: 18-80 years Sexes eligible for study: both Accepts healthy volunteers: no Inclusion criteria: adult patients (18-80 years), patients presenting for ophthalmological surgery under general anaesthesia, ASA I and II, able to communicate in English, Setswana or Afrikaans.

Data category	Information
	Exclusion criteria: ASA III and above, contra-indications to Laryngeal Mask Airway use during general anaesthesia, severe medical or surgical conditions who are expected to have prolonged admissions or ICU admissions, uncontrolled psychiatric conditions, known allergy or adverse reaction to volatile anaesthetics, known or suspected susceptibility to Malignant Hyperthermia, incomplete records, patients who are not treated according to the prescribed treatment protocol.
Study type	Interventional Allocation: randomised Masking: double blind (patient and observer)
Date of first enrolment	February 2020
Target sample size	180
Recruitment status	Recruiting
Primary outcome(s)	To evaluate whether there is a difference between post-operative quality of recovery in patients who received desflurane and in patients who received isoflurane for maintenance of anaesthesia, using the QoR-15 score, a patient-rated outcome measure.
Key secondary outcomes	• To compare the consumption and relative cost of using isoflurane vs desflurane with a minimal or basal flow anaesthetic technique. • To evaluate the difference in time spent in the recovery room between the two patient groups will also be compared.

1.2 Revision Chronology

Date	Protocol Amendment Number	Description
1 Nov 2018	1	Original
8 April 2019	2	Amendments after first review by SMU School Research Committee, formatted according to SPIRIT Statement 2013. Change in title and development of acronym.
14 Feb 2020	3	Updated Standard Anaesthesia Treatment Protocol, Updated Case Report Form: Data Collection, Included results from

		Feasibility Questionnaire and Pilot Study. Included details of registration with ClinicalTrials.gov.
10 Oct 2020	4	Updated title: Removed “Dr George Mukhari Academic Hospital”, replaced with “a Tertiary Hospital”. This was requested by the SMU Research Ethics Committee to make the research more generalizable.
19 April 2021	5	Added SAHRA reference number for notification of Phase IV trial. Adjusted time-line, which has been affected severely by the COVID-19 pandemic.

1.3 Roles and Responsibilities

CS conceived of the study and wrote the protocol. HK acted as supervisor and guided the process.

CS will be responsible for obtaining funding through research grants.

CS will be responsible for the overall conducting of the trial: including recruitment, training and liaising with treating anaesthetists and the research assistant, data collection and analysis and writing up the trial for publication.

1.4 Funding

- Expenses = **R 51 037**:
    - Statistician fee (including: data plan, data analysis and randomisation service): R 5 000
    - Desflurane (6 bottles): R 9 537 (incl. VAT)
    - Translation costs: R 3 500
    - Printing costs: R 3 000
    - Research assistant: a research assistant will be paid R100 per hour to visit the patient post-operatively in order to complete the QoR, as well as to read the data into REDCap.
        - Estimated 2 hours per day, 25 days per month, for 6 months = R30 000
- Income:
    - Abbvie Scholarship: **R 10 000**
        - The chief researcher is a current recipient of the Abbvie Scholarship.
    - JPRF application: **R50 000**

- The chief researcher was successful in the application for funding from the SASA Jan Pretorius Research Fund. (Grants are made to deserving members of SASA for clearly defined research projects, which are acceptable to SASA and fall within the scope of Anaesthesia.)

1.5 Timeline

8 November 2018	Submission to School Research Committee
April 2019	Submission of revised protocol to School Research Committee
July 2019	Submission to SMU Research Ethics Committee
October 2019	Approval obtained from SMUREC: SMUREC/M/240/2019:PG
December 2019	Trial registered with ClinicalTrials.gov: NCT04188314
January- February 2020	Pilot Study (10 patients)
Early February 2020	Review results of pilot study
February 2020	Start data collection
March 2020	Covid-19 Pandemic starts
October 2020	Data collection resumes
July 2021	End data collection
August 2021	Analyse data
September 2021	Write dissertation and article for publication
October 2021	Submit dissertation for evaluation

2 Introduction

2.1 Background

2.1.1 Study Problem and Research Question

Recovery after surgery and anaesthesia has traditionally been assessed with objective measures including time to awakening, time to regaining airway reflexes, duration of stay in the recovery room and/or hospital, and incidence of adverse events like pain and post-operative nausea and vomiting. Increasingly, the patient's experience of their post-operative recovery is being recognised as an important outcome after surgery. The 15-Item Quality of Recovery score (QoR-15) has been validated to give a patient-centred global measure of overall health status after surgery and anaesthesia (1,2). This score has recently been translated and validated in isiZulu (3).

Desflurane is the newest anaesthetic vapour to market, with many benefits from the anaesthetist's perspective: faster time to awakening, faster time to regaining airway reflexes, and a clearer sensorium post-operatively. However, there is a paucity of data evaluating whether this translates to better quality of recovery for the patient. Desflurane is more expensive than other volatiles; for economic use, it is recommended to use Desflurane with a low flow (up to 2L) anaesthetic technique.

Isoflurane is the most commonly used volatile anaesthetic agent at Dr. George Mukhari Academic Hospital. Concerns about the increased cost of desflurane compared to isoflurane limits the use of this novel agent in the public sector in South Africa. Following an extensive literature review, no studies could be found comparing quality of recovery between desflurane and isoflurane using a validated quality of recovery tool like the QoR-15.

The **research question** in this study is whether there is a clinically significant difference in post-operative quality of recovery (using the QoR-15 score) between desflurane and isoflurane inhalational anaesthesia in adult patients presenting for elective ophthalmological surgery under general anaesthesia.

This study will therefore compare quality of recovery between desflurane and isoflurane inhalational anaesthesia. Furthermore, the study will evaluate the relative cost of using either volatile with a minimal or basal flow anaesthetic technique.

2.1.2 Literature Review

The ideal volatile anaesthetic should be potent, with a low solubility in blood and tissues, which should promote fast onset and offset of the drug effect. It should provide safe, effective and reliable anaesthesia with minimal side-effects. The agent must be able to resist physical and metabolic degradation, and it should not pose a threat to the environment (4). Preferably, it should also be cost-effective and simple to use. One aspect that is often overlooked in the description of the "ideal anaesthetic agent", is the quality of recovery from the patient's point-of-view.

Isoflurane is the most commonly used inhaled anaesthetic agent at Dr. George Mukhari Academic Hospital. Desflurane has recently become available. Both agents are indicated for maintenance of anaesthesia. Neither agent is indicated for induction of anaesthesia, as they are pungent and irritating to the airways.

The side-effect profiles of the two vapours are similar. Both agents may cause respiratory irritation (coughing, bronchospasm, laryngospasm) and respiratory depression. Both agents may cause myocardial depression and hypotension in a dose-dependent fashion. Desflurane may cause a transient, indirect stimulation of the sympathetic nervous system which may arise from stimulation of rapidly adapting upper airway receptors. Isoflurane may also cause emergence reactions, cardiac arrythmias, involuntary muscle movements and

hiccupping. Both agents may cause post-operative shivering, nausea and vomiting, as well as leucocytosis (even in the absence of surgical stress). Both agents may interact with carbon dioxide adsorbents to form carbon monoxide, especially when the adsorbent dries out; carbon monoxide inhalation may lead to formation of carboxyhaemoglobin in exposed patients (5–7).

Both Isoflurane and Desflurane are contra-indicated in patients who may be susceptible to Malignant Hyperthermia or to auto-immune hepatitis. Isoflurane should be avoided in patients with cerebral space occupying lesions or raised intracranial pressure. Both agents will be contra-indicated when general anaesthesia is contra-indicated.

“Recovery” and “Quality of Recovery” are complex, abstract concepts, lacking in universally accepted definitions. In basic terms, “Recovery” can be seen as a return to the patient’s pre-operative state, or indeed, to an improved state. This is dependent on patient, surgical and anaesthetic factors. “Quality of Recovery” is a patient-centred concept, and several valid and reliable instruments have been developed that take into account physical and mental well-being factors that impact on the patient’s experience of their recovery (8).

Quality of recovery should be distinguished from patient satisfaction. Whether quality of recovery has an impact on patient satisfaction is unclear (9). Patient expectations, cultural and social background and cognitive factors all impact on patient satisfaction. Tools evaluating patient satisfaction emphasise the following: information provided to the patient, physical comfort, involvement in care, emotional support and privacy (8).

Recovery after inhaled anaesthesia has mostly been evaluated by parameters related to speed of emergence from anaesthesia, for example: time to open eyes, time to respond to command, time to remove LMA, and time to state date of birth. For all of these parameters, the time to effect is significantly shorter for desflurane compared to sevoflurane, isoflurane and propofol (4,10,11).

Some studies have evaluated later end-points of recovery including level of activity and side-effects on the day after surgery. Mahmoud et al (12) evaluated female patients who underwent laparoscopic gynaecological day-case surgery with either sevoflurane or desflurane for maintenance of anaesthesia; they found that the patients who received desflurane had greater return to normal activity the day after surgery compared to the sevoflurane group. This was done using a semi-structured telephonic questionnaire. White et al (13) found no difference in later end-points of recovery between sevoflurane and desflurane in patients undergoing superficial surgical procedures. This was assessed with a telephonic interview the day after surgery. This trial also included a basic assessment of patient satisfaction with their anaesthetic experience on a 3-point rating scale: 0 = dissatisfied, 1 = satisfied and 2 = highly satisfied. There was no difference in satisfaction between the two groups.

Studies comparing desflurane and isoflurane have been done, most also focussing on parameters relating to emergence from anaesthesia, as stated above. Emergence has been found to be faster for patients receiving desflurane; a finding that holds true for obese and elderly patients (4). Many of the early studies aimed for alveolar concentrations in excess of 1x the minimum alveolar concentration (MAC) of the volatile agents, which may explain the greater incidence of adverse reactions seen with desflurane. Jakobsson et al (14) compared desflurane and isoflurane anaesthesia in patients undergoing laparoscopic gynaecological surgery. Their study confirmed shorter time to emergence with desflurane, including time to extubation and return of cognitive function, and similar rates of post-operative nausea and vomiting and pain. Patients were asked to rate the quality of anaesthesia as “good – better than expected” or “bad – worse than expected”. There was no significant difference between the two groups.

A systematic review published in 2004 comparing the recovery profiles after ambulatory anaesthesia with propofol, isoflurane, sevoflurane and desflurane, included 4 studies comparing desflurane and isoflurane. Unfortunately, none of the studies included in the review reported on later end-points of recovery or quality of recovery (15).

Few studies comparing volatile anaesthetic agents used validated quality of recovery tools. One study, reported in German in 2011, used the QoR-40 at 24 hours to evaluate differences between anaesthesia with desflurane and sevoflurane. Though parameters for early postanaesthetic recovery were superior in the patients receiving desflurane, there was no difference in the QoR-40 after 24 hours (16). A recently published randomised controlled trial primarily evaluating the effects of desflurane, sevoflurane and propofol on emergence times and airway reactions, evaluated patient responses to the Post-operative Quality of Recovery Score (PQRS) as a secondary outcome, and found no difference in quality of recovery between the groups (11).

Numerous tools have been developed in recent years to evaluate the quality of recovery from the patient’s perspective (8). Multi-dimensional scales like the 24h Functional Ability Questionnaire (24h-FAQ), Postoperative Recovery Profile, Postoperative Quality of Recovery Scale (PQRS), Functional Recovery Index (FRI), and the 40-Item and 15-Item Quality of Recovery Scores (QoR-40 and QoR-15) have demonstrated comprehensive postoperative outcome results. The recent systematic review by the StEP-COMPAC group (Standardized Endpoints for Perioperative Medicine, Core Outcomes Measures in Perioperative and Anaesthetic Care) recommended one or more of six defined end-points be used in clinical trials assessing patient comfort after surgery (17). The QoR-15 is included in this list of six end-points: pain intensity at 24 h postoperatively, nausea and vomiting, one of two quality-of-recovery (QoR) scales (QoR score or QoR-15), time to gastrointestinal recovery, time to mobilisation, and sleep quality. The systematic review by Kleif et al (2) also recommends that the QoR-15 be used as a standard measure of quality of recovery in clinical trials in surgery and anaesthesia.

Previously, the QoR-40 was recommended as a global measure to assess the patient's experience of their overall health status after surgery and anaesthesia, but it takes around 10 minutes to complete. The QoR-15 was developed as an abbreviated version of the QoR-40, that would be more feasible in research and clinical practice; this questionnaire can be completed in less than 3 minutes (1).

The QoR-15 is a 15-item post-operative score evaluating both physical and mental well-being by assessing five dimensions: emotional state, physical comfort, psychological support, physical independence and pain. Each of the 15 items are scored by the patient from 0 (worst score) to 10 (best score), giving a lowest possible score of 0, and a highest possible score of 150. This continuous composite score allows comparisons between intervention groups. The minimal clinically important difference (MCID) and patient acceptable symptom state score for the QoR-15 score has been determined: the MCID is 8 and the acceptable symptom state score is 118 (18). The QoR-15 has good scaling properties, and during development and testing the scores followed a normal distribution (1).

The QoR-15 has undergone extensive validation and psychometric evaluation. The English and translated versions have been found to have good validity and reliability in assessing quality of recovery (2). During development and testing, the QoR-15 was able to discriminate between men and women. This is important as it has previously been shown that women generally have a worse post-operative experience. The QoR-15 furthermore showed a negative correlation with duration of surgery, duration of time spent in the post-anaesthesia care unit, and duration of hospital stay (1).

During an extensive review of the literature, no studies could be found comparing quality of recovery between desflurane and isoflurane using a validated quality of recovery tool like the QoR-15. Isoflurane is the most commonly used volatile anaesthetic agent at Dr. George Mukhari Academic Hospital. Desflurane is being introduced into our practice, and it remains to be seen if it holds benefits with regards to patient-rated quality of recovery.

2.2 Aim and Objectives

2.2.1 Aim

This study will compare quality of recovery between desflurane and isoflurane inhalational anaesthesia.

2.2.2 Primary Objective and Hypothesis

The primary objective of the study is to evaluate whether there is a difference between post-operative quality of recovery in patients who received desflurane and in patients who received isoflurane for maintenance of anaesthesia, using the QoR-15 score, a patient-rated outcome measure.

Isoflurane is the standard drug used in our setting for maintenance of anaesthesia and will therefore be used as the drug for the control group. Desflurane will be used as the interventional drug.

The minimal clinically important difference for the post-operative QoR-15 has been found to be 8. In other words, an intervention that changes the mean post-operative score by 8, can be interpreted to signify a clinically important improvement or deterioration.

The null hypothesis for this study is that there is no statistically significant difference in mean post-operative QoR-15 scores of patients receiving isoflurane and desflurane for maintenance of anaesthesia. The alternative hypothesis is that there is a statistically significant difference in mean post-operative QoR-15 scores between patients receiving isoflurane and desflurane.

2.2.3 Secondary Objectives

A secondary objective will be to compare the consumption and relative cost of using isoflurane vs desflurane with a minimal (0.25-0.5 ml/min) or basal (0.2-0.25 ml/min) flow anaesthetic technique. This will be done by comparing the amount of vapour used in millilitre per hour between desflurane and isoflurane during minimal or basal flow anaesthesia. The relative cost of the vapour used will be estimated, based on the current government purchase price of isoflurane and desflurane.

Furthermore, the difference in time spent in recovery between the two patient groups will also be compared.

3 Methodology

3.1 Trial Design

This study will be conducted as a randomised, controlled, patient and observer blinded, single-centre trial with two parallel groups and a primary end-point of 15-point Quality of Recovery Score on day 1 after surgery. Randomization will be performed as block randomization with a 1:1 allocation.

3.2 Participants, Interventions and Outcomes

3.2.1 Study Setting

The study will be conducted in the theatre complex at Dr. George Mukhari Academic Hospital, a tertiary training centre affiliated with Sefako Makgatho Health Sciences University. Specifically, the study will be conducted in the ophthalmological theatre, on patients undergoing ophthalmological surgery under general anaesthetic.

The decision to use patients for ophthalmological surgery is based on the consideration that the procedures last an average of 1 hour, the patients are usually systemically well, the anaesthetic technique can be standardised for all patients, the surgery itself is unlikely to lead to poor quality of recovery and the patients are unlikely to require high doses of opioids for analgesia. Review of the theatre records for the ophthalmology theatre revealed that 166

patients between the ages of 18-87 years underwent general anaesthesia in the 6 months between 1 March – 31 August 2018. Mean age was 42 years, with 150 patients in the age range 18-65 years. Mean duration of surgery was 74 minutes (range: 20-180 minutes), with 141 cases lasting 40-120 minutes.

3.2.2 Eligibility Criteria

Inclusion Criteria:

- Adult patients between the ages of 18-80 years of age.
- Patients presenting for ophthalmological surgery under general anaesthesia.
- ASA I and II.
- Able to communicate in English, Setswana or Afrikaans.

Exclusion Criteria:

- Patients outside the specified age range.
- ASA III and above.
- Patients with contra-indications to Laryngeal Mask Airway use during general anaesthesia.
- Patients with severe medical or surgical conditions, who are expected to have prolonged admissions or ICU admissions.
- Patients with uncontrolled psychiatric conditions like depression, schizophrenia, mania, dementia.
- Patients with known allergy or adverse reaction to volatile anaesthetics.
- Patients with known or suspected susceptibility to Malignant Hyperthermia.
- Patients with incomplete records (Data Collection Form and QoR-15).

3.2.3 Interventions

The control group will receive isoflurane for maintenance of anaesthesia. The intervention group will receive desflurane for maintenance of anaesthesia.

Standard protocols for induction and maintenance of anaesthesia will be followed, as discussed with Prof. F. Puehringer, an international expert in the field of desflurane use. A detailed leaflet describing the protocol has been developed (see Appendix 6.5), which will be handed to the treating anaesthetist on the day of surgery.

- Confirm anaesthetic workstation has passed the machine check, and record any machine leak, if present.
- Intravenous Induction of Anaesthesia:
    - Fentanyl 1.5-3 mcg/kg pre-induction to reduce airway responses during manipulation. Lower doses to be used for short procedures and larger dose for longer procedures.
    - Lignocaine 40 mg pre-induction to minimize Propofol-induced injection pain.

- Propofol 2-2.5 mg/kg until induction of anaesthesia.
- Dexamethasone 8mg after induction of anaesthesia to prevent post-operative nausea and vomiting and to decrease opioid requirements.
- Mask ventilation with 6 l/min 100% oxygen until airway is placed.
- Airway management will be with a Laryngeal Mask Airway (LMA), size selected according to patient weight.

- Use of Muscle Relaxants During Procedure:
  - If required, a small dose of muscle relaxant may be administered to facilitate immobility during the procedure.
  - For Rocuronium, a dose of up to 0.15mg/kg may be used (about 10-15mg for most adults). This dose is a quarter of the normal intubating dose for Rocuronium.
  - For Cisatracurium, a dose of up to 0,05mg/kg may be used (about 2.5 – 4mg for most adults). This dose if a quarter of the normal intubating dose for Cisatracurium.
  - Top-up doses may be given every 30-40 minutes, if required; dosing should be the same as the initial dose.
- Maintenance of Anaesthesia:
  - Isoflurane:
    - After the airway is secured, fresh gas flow is reduced to 2 l/min and the Isoflurane vaporiser is opened and adjusted to attain 1MAC.
    - Once 1MAC is attained, the fresh gas flow will be reduced to 0.2-0.5 l/min and the vaporiser will be adjusted to maintain 1MAC. The aim will be to reduce the fresh gas flow as low as possible, taking into consideration the amount of machine and/or circuit leak.
    - If basal flow (0.2L/min) is reached, FiO2 will be set to 100% to meet the patient's oxygen demand.
    - Should the bag on the anaesthetic machine collapse during minimal or basal flow anaesthesia (e.g. because of a poor seal from the LMA, or due to circuit leak) the following steps should be taken: increase the fresh gas flow to 2 L/min and adjust the vaporiser concentration to maintain 1MAC, allow the bellows to fill and then return to the previous concentration and fresh gas flow settings.
  - Desflurane:

        - After the airway is secured, fresh gas flow is reduced to 2 l/min and the desflurane vaporiser is opened to 12%. This is maintained until 1MAC is reached, usually about 3-5 minutes.
        - The fresh gas flow will then be turned down to 0.2-0.5 l/min and the vaporiser adjusted to maintain 1MAC. The aim will be to reduce the fresh gas flow as low as possible, taking into consideration the amount of machine and/or circuit leak.
        - If basal flow (0.2L/min) is reached, FiO2 will be set to 100% to meet the patient's oxygen demand.
        - Should the bag on the anaesthetic machine collapse during minimal or basal flow anaesthesia (e.g. because of a poor seal from the LMA, or due to circuit leak) the following steps should be taken: turn the vaporiser concentration to 12% and the fresh gas flow to 2 L/min, allow the bellows to fill and then return to the previous concentration and fresh gas flow settings.
    - The use of minimal or basal fresh gas flow is intentional, to minimise the amount of anaesthetic vapour used. When basal flow is used, 100% oxygen is required to meet patient's oxygen demand.

- Managing Potential Problems:
    - Should the ophthalmologist complain that the patient is in too light a plane of anaesthesia, the patient may be deepened with a bolus of Propofol 0.5-1 mg/kg.
    - For intra-operative analgesia (for example if patient develops tachycardia or hypertension), administer 50mcg Fentanyl boluses intravenously.
    - When post-operative analgesia is required, administer 50-100mg of Tramadol intravenously as a bolus 20 minutes before the end of the procedure.
    - For post-operative nausea or vomiting (only if required), administer 4mg of Ondansetron intravenously as a bolus, followed by 10mg of Metoclopramide after 30 minutes (only if further treatment is required).
- End of Procedure:
    - If a small dose of muscle relaxant was used, the effects should be reversed with Neostigmine 0.04mg/kg (2-3mg for most adults) 10-20 minutes before the end of the procedure. Glycopyrrolate or Atropine may be added to prevent bradycardia and gastro-intestinal side-effects.
    - The vaporisers will be closed, and fresh gas flow will be increased to 6 l/min in order to wash out the volatile anaesthetic.
- Recovery and Discharge

- The patient will be taken to the recovery room when they are able to protect their airway, as per normal practice.
- Discharge from the recovery room to the ward will be according to the standard procedures in the post-anaesthesia recovery room. Patients should score at least 9 on the modified Aldrete score, with the patient awake and alert with stable vital signs, not experiencing any acute side effects (e.g., nausea or vomiting) or moderate-to-severe pain.

3.2.4 Materials, Apparatus and Instruments

Basic Materials and Apparatus:

- Patients will be induced in the ophthalmology theatre; anaesthesia will be maintained with the Datex-Ohmeda Aisys CS2 anaesthetic workstation.
- Isoflurane is freely available, and the standard anaesthetic vapour that is used in our setting.
- Desflurane will be purchased for use in the study.
- Vaporisers for both isoflurane and desflurane are available in our theatre complex.
- Nitrous Oxide will not be used as part of the fresh gas mixture, because it is not always available in our setting.
- Standard monitors will be used during anaesthesia: non-invasive blood pressure monitoring, pulse oximetry, 3-lead electrocardiogram, capnography and gas analysis.

Instruments:

Quality of Recovery will be measured with the 15-Item Quality of Recovery score (QoR-15):

- The English version can be used for English-speaking patients. There is no copyright on the form (confirmed by the author, Prof. P.S. Myles via email).
- The form will be translated into Afrikaans and Setswana.
  - Forward translation has been done in advance by an accredited medical translator at Zwelinhle Translation Services.
  - Back translation of both translations has been done by a separate panel of health care professionals, who were blinded to the original English version. Three Setswana home language speakers did the back-translation for the Setswana version, and three Afrikaans home language speakers did the back-translation for the Afrikaans version.
  - The final versions have been corrected and adapted by all panel members.
  - See Appendices 6.9 and 6.10 for the translated versions.

- The QoR-15 is a validated and reliable tool for measuring quality of recovery. The patient is asked to rate their experience of 15 items from 0 (worst score) to 10 (best score).
- Where possible, the QoR-15 form will be handed to the patient to complete by themselves. However, in cases where patients are visually impaired, the items on the questionnaire will be read to them, and their responses recorded.

3.2.5 Feasibility

Consensus on the **acceptability feasibility** of the treatment protocol has been obtained from peers and colleagues in the Department of Anaesthesia by circulating the proposed standardised treatment protocol (see Appendix 6.5) and asking for feedback.

Eleven feasibility questionnaires were completed (See Appendix 6.2 for template of the questionnaire). All 11 respondents indicated that they thought the protocol to be practical and easy to follow. All 11 respondents indicated that they would be comfortable giving anaesthesia according to the treatment protocol. Five respondents have never used Desflurane before in clinical practice; of these 3 respondents were subsequently taught how to use Desflurane during a training workshop, the other 2 respondents were instructed on the use of Desflurane by the Chief Researcher during clinical cases.

Most of the concerns recorded on the forms related to the use of basal fresh gas flow. One responded commented that the technique is labour-intensive and user-dependent. The same respondent was concerned about flushing the circuit with oxygen only when the bellows collapse, as this may lead to a drop in MAC, which may cause the patient to be in too light a plane of anaesthesia. One respondent was concerned about using basal flow with a Laryngeal Mask Airway, as there may be a leak if the airway does not seal properly. Another respondent was concerned about using basal fresh gas flow with the Drager Perseus anaesthetic workstation, as the bag tends to collapse when fresh gas flows below 0.6 l/min are used. One consultant anaesthetist was concerned about potential for carbon dioxide retention with basal flow anaesthesia and exhausted carbon dioxide absorber. These concerns are addressed in the changes to the treatment protocol – see below. One respondent was concerned about laryngospasm and bronchospasm – this is rarely a problem when Desflurane is used according to the recommended protocol with a maximum fresh gas flow of 2L and maximum vaporiser concentration of 12%.

Practicality feasibility of the standardised anaesthesia treatment protocol has been tested in a pilot of ten cases. Initially four cases were selected for the pilot study, but after these cases changes were made to the standardised treatment protocol, and a further six cases were piloted to ensure all concerns and issues had been addressed in the amended treatment protocol. Two of the further six cases received Sevoflurane instead of Isoflurane or

Desflurane; one case due to the treating anaesthetist not receiving the message about the study in time, the other case due to the patient requesting a gas induction. An additional two pilot cases were done, bringing the total number of pilot cases to 12. The cases for the pilot were not randomised and will not be included in the final study data. Isoflurane was used for three pilot cases and desflurane was used for seven pilot cases (the two sevoflurane cases were not counted). It was decided to increase the number of Desflurane pilot cases to ensure the treating anaesthetists had enough exposure to using the newer agent before starting the actual trial.

For the first four pilot cases the Chief Researcher went to assess the patients pre- and post-operatively. Two of the patients had already been discharged by the time the Chief Researcher went to their wards. This confirmed the need for a research assistant to see the patients post-operatively before discharge. It was also not possible for the Chief Researcher to be blinded to the anaesthetic agent used, as she assisted the treating anaesthetists during induction. In one of the pilot cases, the patient developed laryngospasm when Desflurane was started after placement of the airway; the likely reason was that low doses of fentanyl and propofol were given during induction. In another case, 3mcg/kg of fentanyl was given at induction, and then the surgeons decided after the examination under anaesthesia that the patient was not for further intervention – it took time for the respiratory depression from fentanyl to wear off. During one of the pilot cases, the consultant anaesthetist in the ophthalmological theatre recommended a small dose of muscle relaxant to assist with patient immobility during delicate surgery.

Having evaluated the acceptability and practicality feasibility, the following **changes** were made to the standard treatment protocol (See appendix 6.6 for the full updated version):

- Treating anaesthetist to test the machine daily, as per standard practice, with a clean circuit. Carbon dioxide absorber should be checked daily and replaced when needed. The treating anaesthetist will record the machine leak as determined during the machine check.
- Allow fresh gas flow of 0.2-0.5 l/min, aiming to reduce the fresh gas flow as low as possible, taking into consideration the machine leak. This change allows the treating anaesthetist to adjust the fresh gas flow according to the amount of leak in the circuit. All responding anaesthetists felt more comfortable with this adjustment to the protocol.
- Steps to take when the bellows collapse: increase the fresh gas flow to 2 l/min and increase the concentration on the vaporiser to maintain 1MAC (maximum 12% for Desflurane). This will prevent a decrease in the MAC from flushing the circuit with oxygen only.
- In some cases, a small dose of muscle relaxant may be used to facilitate immobility during the procedure. The dose of muscle relaxant will be limited to 25% of the intubating dose, and reversal with neostigmine (plus glycopyrrolate or atropine) is mandatory. Glycopyrrolate is preferred, but it is currently out of stock.

This small dose of muscle relaxant should not affect the patient's post-operative quality of recovery, especially if it is reversed.

- Dose of Fentanyl changed to 1.5-3mcg/kg, to allow for smaller doses to be given for short procedures lasting 30 minutes or less.
- In cases where post-operative pain is expected, the treating anaesthetist may administer 50-100mg Tramadol 20 minutes before the end of the procedure, rather than waiting until the patient was in the recovery room.
- The anaesthetic workstation in the ophthalmology theatre has been changed to a Datex-Ohmeda CS2, which gives a clear indication of the amount of circuit leak after the machine check, and experience has shown that it has a smaller baseline leak than the Drager Perseus workstation.

The changes made to the standardised anaesthesia treatment protocol makes it more practical and pragmatic, and it will improve adherence to the study protocol. This will prevent exclusion of cases which were not treated according to the study protocol.

3.2.6 Outcomes

Primary outcome measures:

- Quality of recovery will be assessed in all participants with the QoR-15 score.
    - A baseline QoR-15 will be measured pre-operatively, and a repeat measurement will be done on day 1 post-operatively before discharge.
    - For each patient, the pre- and post-operative QoR-15 scores will be recorded, as well as the difference between the two measurements. The mean and median differences between the pre- and post-operative QoR-15 scores of the control group and the intervention group will be compared and tested for significance.
    - The mean and median post-operative QoR-15 scores of the control group and the intervention group will be compared and tested for significance.

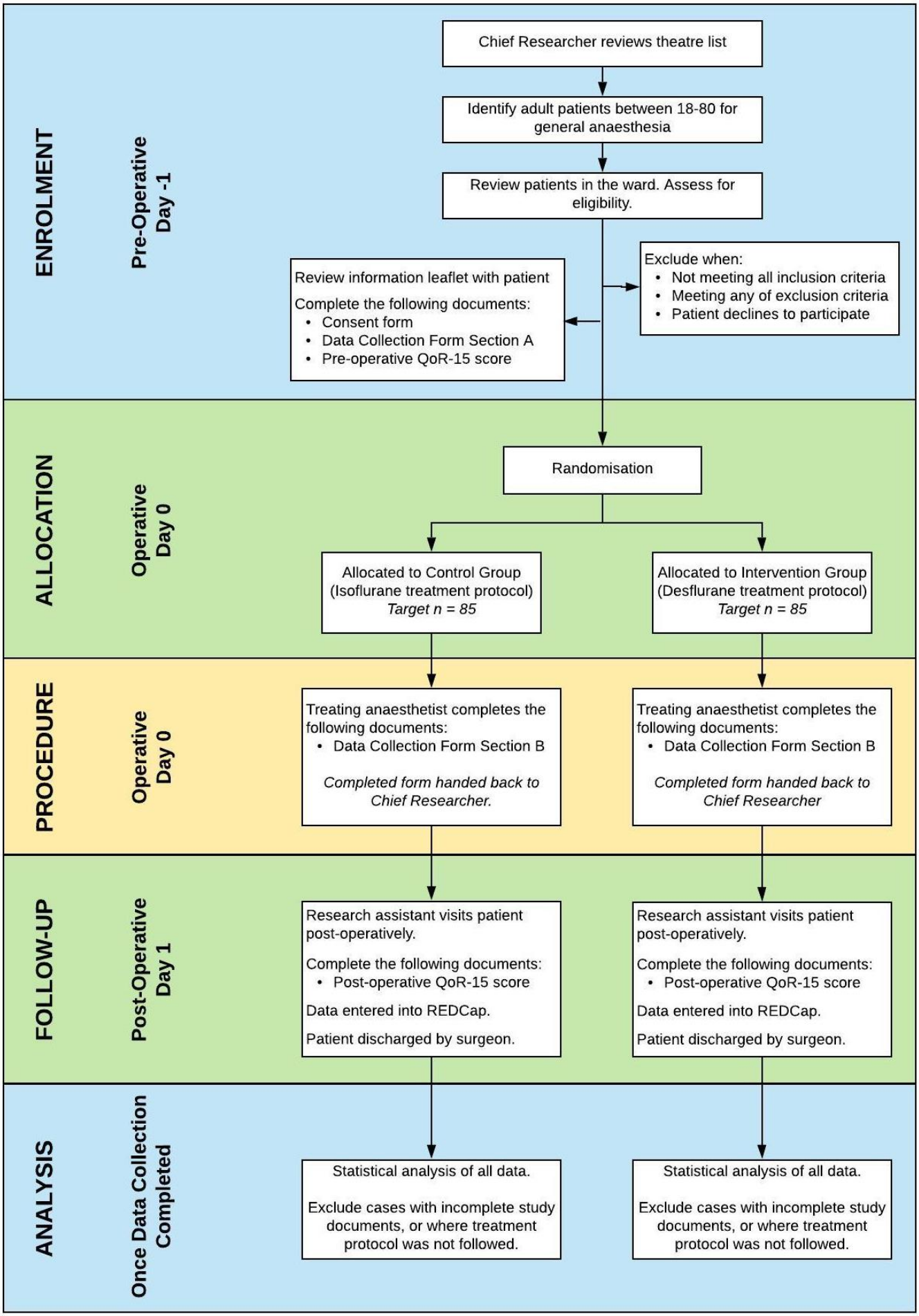
Secondary outcome measures:

- To evaluate the consumption and cost of isoflurane and desflurane with a minimal or basal anaesthetic technique:
    - The vapour use per case in millilitres will be recorded from the anaesthetic machine.
    - The purchase price for isoflurane and desflurane will be obtained from the pharmacy.
    - The mean and median consumption of vapour between the two groups will be compared.
    - The mean and median cost of isoflurane and desflurane will be compared.

- To evaluate time in recovery:
    - The time the patient enters and leaves the recovery room will be recorded, as well as the total time the patient spends in the recovery room.
    - The mean and median time spent in recovery will be compared between the two groups.

3.2.7 Participant Timeline and Flow-Diagram

	STUDY PERIOD				
	Enrolment	Allocation	Post-allocation		Close-out
TIMEPOINT:	Day -1	Day 0	Day 0	Day 1	
ENROLMENT					
Eligibility screen:	X				
Informed consent:	X				
Data Collection Form Section A:	X				
ALLOCATION		X			
INTERVENTIONS					
Isoflurane protocol:			X		
Desflurane protocol:			X		
ASSESSMENTS					
Pre-Operative QoR-15:	X				
Post-Operative QoR-15:				X	
Vapour Consumption (ml):			X		
Time in Recovery (min):			X		
DATA ANALYSIS					X


ENROLMENT
Pre-Operative Day -1
Chief Researcher reviews theatre list
Identify adult patients between 18-80 for general anaesthesia
Review patients in the ward. Assess for eligibility.
Exclude when:
• Not meeting all inclusion criteria
• Meeting any of exclusion criteria
• Patient declines to participate
Review information leaflet with patient
Complete the following documents:
• Consent form
• Data Collection Form Section A
• Pre-operative QoR-15 score
ALLOCATION
Operative Day 0
Randomisation
Allocated to Control Group (Isoflurane treatment protocol) Target n = 85
Allocated to Intervention Group (Desflurane treatment protocol) Target n = 85
PROCEDURE
Operative Day 0
Treating anaesthetist completes the following documents:
• Data Collection Form Section B
Completed form handed back to Chief Researcher.
Treating anaesthetist completes the following documents:
• Data Collection Form Section B
Completed form handed back to Chief Researcher
FOLLOW-UP
Post-Operative Day 1
Research assistant visits patient post-operatively.
Complete the following documents:
• Post-operative QoR-15 score
Data entered into REDCap.
Patient discharged by surgeon.
Research assistant visits patient post-operatively.
Complete the following documents:
• Post-operative QoR-15 score
Data entered into REDCap.
Patient discharged by surgeon.
ANALYSIS
Once Data Collection Completed
Statistical analysis of all data.
Exclude cases with incomplete study documents, or where treatment protocol was not followed.
Statistical analysis of all data.
Exclude cases with incomplete study documents, or where treatment protocol was not followed.

3.2.8 Sample Size

Sample size calculation is based on estimation of the difference in mean post-operative Quality of Recovery (QoR) scores, after anaesthesia with desflurane or isoflurane. With a sample size of 85 in each group, a two-sided two-sample t-test at the 5% significance level, will have 80% power to detect a difference of 8 between the mean post-operative QoR scores with desflurane and isoflurane, assuming a standard deviation of 18.5, Sample size calculation was done on nQuery Advanced (Statistical Solutions Ltd, Cork, Ireland), Release 8.0.

A sample of 170, randomised in a 1:1 ratio to treatment with desflurane and isoflurane (85 per group) is proposed for this study.

3.2.9 Recruitment

Recruitment will be done by the Chief Investigator. The following steps will be followed:

1. Review the theatre booking list for theatre 11 the day before surgery.
2. Identify adult patients between the ages of 18 and 80 on the list, scheduled for general anaesthesia.
3. Review the patients in the ward:
    a. Screen for any exclusion criteria.
4. Once confirmed that there are no exclusion criteria:
    a. Explain the objectives of the study to the patient.
    b. Hand the patient a patient information leaflet and discuss any questions the patient may have.
    c. Take informed consent if the patient agrees to participate in the study.
5. Record the patient's name on a sequentially numbered list. This will be the only document to contain any personal information of the patient. It will be stored securely by the Chief Researcher. The number on the list will be the patient's study number and this number will be recorded on all study documents.

3.3 Assignment of Interventions

3.3.1 Allocation and Randomisation

Patients will be randomly allocated to either the control or the intervention group by computer randomisation. Randomisation and allocation will be managed remotely by the statistician, who will not be involved in patient care, and who will only gain access to study data after completion of data collection.

Block randomisation will be done to ensure that an equal number of patients are assigned to each treatment arm. Random block sizes will be used and the chief investigator, research assistant and treating anaesthetists will be blind to the size of each block.

Sequentially numbered, sealed, opaque envelopes will be prepared by the statistician. This will include a piece of paper indicating the group the patient has been randomised to. The sealed envelope will be handed to the treating anaesthetist on the day of surgery by the Chief Researcher. The Chief Researcher will be responsible for enrolment and assignment of participants.

3.3.2 Blinding

The patient will be blinded to the group they have been randomised to, as the vapour will only be started after induction of anaesthesia. The research assistant administering the post-operative QoR-15 will be blinded to the intervention.

The treating anaesthetist, the Chief Researcher and theatre staff will not be blinded to the intervention, as this would not be practical. All treating anaesthetists and theatre staff will be strongly inculcated not to disclose the allocation status of the participant at any time prior or after the general anaesthetic.

The piece of paper indicating the group will be attached to the Case Report Form. The Case Report Form will be collected by the Chief Researcher and will not be in the patient's file where it may unblind the patient or research assistant.

There are no circumstances under which unblinding will be permissible.

3.4 Data Collection

3.4.1 Source Documents

The following documents will be used as original source documents from which patient information will be gathered:

- Patient file: history, vital signs, comorbidities, previous anaesthesia and complications.
- Theatre booking list: patient age, type of anaesthesia.
- Blue anaesthetic report card: complete record of the anaesthesia care to the patient.
- Theatre record book: anaesthesia times, basic record of medications given.
- Nursing theatre record: anaesthesia times, recovery times, basic record of medications given.
- Stored history on the Datex-Ohmeda Aisys CS2 workstation in theatre 11: vapour consumption, anaesthesia times.

3.4.2 Study Documents

The following documents will be used as study documents to record relevant information:

- Case Report Forms (CRF)
    - CRF: Data Collection

- CRF: Pre-operative QoR-15 form
- CRF: Post-operative QoR-15 form

- Consent Form
- Patient Information Leaflet
- Standardised Anaesthesia Protocol

The templates for all the above documents are added to this protocol as Appendices.

3.4.3 Data Collection Procedures

Patients will be assessed by the chief researcher pre-operatively on the day before surgery. The demographic information on the Data Collection Form (Section A) will be completed. Information will be obtained from the patient's file, as well as from an interview with the patient. The chief researcher will accurately measure the patient's weight and height with the available scales and measuring devices in the wards.

Patients will then be asked to complete the QoR-15 in the language of their choice, as a measure of health status over the previous 24 hours. Where possible, the QoR-15 form will be handed to the patient to complete by themselves. However, in cases where patients are visually impaired, the items on the questionnaire will be read to them, and their responses recorded.

The following day, the treating anaesthetist will complete the information about the procedure in Section B of the Data Collection Form: anaesthetic time, amount of vapour used, additional medication administered, recovery time, any adverse events (bronchospasm, laryngospasm, post-operative nausea and vomiting and/or other), and whether the prescribed anaesthetic protocol was followed.

Post-operatively, a blinded observer (research assistant) will review the patient on the day following their surgery, prior to discharge. The patients will complete the QoR-15 again.

As follow-up will be done before discharge, retention of patients to follow-up should not present any difficulties.

3.5 Data Management

3.5.1 Database Entry

All study documents will be printed. All data will be recorded by hand on paper forms. After recruitment, the Chief Researcher will record the sequential study number on all documents relating to a particular patient.

The data will be captured electronically on the REDCap database by the research assistant (19). REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data

manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Data from each patient will be captured on REDCap sequentially so that the study number correlates with the database entry number.

3.5.2 Data Storage

Study documents will be stored securely by the Chief Researcher. Documents will be kept in a dedicated lever-arch file and will be arranged sequentially according to study number. All study documents relating to a single patient will be stored together.

3.5.3 Data Inspection

In case of incomplete data in Section B of the Data Collection Form, the chief researcher will review the following source documents in the order listed to obtain the information:

Missing data on medication given intra-operatively:	1. Blue anaesthesia report card 2. Nursing theatre record 3. Theatre record book
Missing data on medication given post-operatively:	1. Blue anaesthesia report card 2. Nursing theatre record
Missing data on anaesthesia start/end times:	1. Blue anaesthesia report card 2. Nursing theatre record 3. Datex-Ohmeda Aisys CS2 stored history 4. Theatre record book
Missing data on vapour start/end times:	1. Blue anaesthesia report card 2. Datex-Ohmeda Aisys CS2 stored history
Missing data on millilitres vapour used:	1. Datex-Ohmeda Aisys CS2 stored history

Patients will complete the QoR-15 forms pre-operatively and post-operatively. The Chief Researcher (pre-operatively) and the research assistant (post-operatively) will review the QoR-15 forms for completeness before leaving the patient's bedside. If the patient omitted any responses, they will be asked to review and complete the form.

3.6 Data Analysis & Statistical Methods

Demographic and clinical characteristics of patients will be summarised descriptively. Continuous variables (e.g. age or weight) will be summarised by mean, standard deviation, median, interquartile range, minimum and maximum values. Categorical variables (e.g. ethnicity or ASA status), will be summarised by frequency count and percentage calculations.

QoR scores will be considered as a continuous variable and will be summarised as above per treatment group (desflurane and isoflurane).

The null hypothesis for this study is that there is no statistically significant difference in mean post-operative QoR-15 scores of patients receiving isoflurane and desflurane for maintenance of anaesthesia. The alternative hypothesis is that there is a statistically significant difference in mean post-operative QoR-15 scores between patients receiving isoflurane and desflurane.

Based on the available literature, it is assumed that the quality of recovery scores will follow a normal distribution. The data will be inspected for normality prior to analysis.

For the primary objective, the mean and median difference in post-operative QoR-15 scores between the two groups will be tested for significance by the two-sided two-sample t-test and the nonparametric Wilcoxon rank sum test respectively. The mean and median difference between the pre-operative and post-operative QoR-15 scores for the two groups will also be tested for significance by the two-sided two-sample t-test and the nonparametric Wilcoxon rank sum test respectively.

For the secondary objectives, mean and median difference in consumption of vapour and time spent in recovery will be tested for significance by the t-test and Wilcoxon test as above.

Analysis, or comparisons, of subgroups of patients may be performed if it would be of clinical interest; for example, if there appears to be a significant difference in QoR scores between male and female patients.

Results will be presented in tables and graphs or verbatim, as applicable.

All statistical analyses will be performed on SAS (SAS institute Inc, Carey, NC, USA), Release 9.4 or higher, running under Microsoft Windows for a personal computer. Statistical tests will be two-sided and p values ≤0.05 (5%) will be considered significant.

3.7 Monitoring

3.7.1 Data Quality Monitoring

The Chief Researcher will periodically monitor the completed study documents and the database entries. If any problems are found with completion of study documents, training sessions will be arranged in the Department of Anaesthesia.

3.7.2 Interim Analysis

Interim analysis will not be done.

3.7.3 Harms

Adverse events will be recorded on the Data Collection Form. The form makes provision for expected adverse events (bronchospasm, laryngospasm, nausea & vomiting and/or other), as well as for unexpected adverse events. Treating anaesthetists will be instructed to report all adverse events to the Chief Researcher as soon as possible.

Both the control and interventional drugs have been extensively studied and used safely in clinical practice. A brief description of their side-effect profiles, which are very similar, can be found in the literature review. It is therefore not foreseen that many unexpected adverse events will occur. The purpose of the study is not to determine frequency or severity of adverse events, but it is acknowledged that adverse events may occur, and therefore monitoring is important.

Patients with known or suspected susceptibility to Malignant Hyperthermia are excluded from participation in the trial. In the unlikely event that a patient presents with signs and symptoms suggestive of Malignant Hyperthermia, treating anaesthetists will be instructed to stop all volatile agents and to follow departmental emergency management protocols.

3.8 Reliability and Validity

- Validity:
    - Internal validity should be assured on the basis that the anaesthetic techniques will be unchanged between the two groups, except for the anaesthetic vapour. Maintaining the end-tidal vapour concentration at 1MAC for both drugs will prevent disproportionate effects of one drug over the other. The patient population should be homogenous, as only ASA I and II patients presenting for ophthalmological surgery will be included in the study.
    - The chief researcher will counsel each treating anaesthetist prior to them starting a study case to ensure that they follow the required standardised anaesthesia protocol. This will reduce the

chance of protocol violations occurring. Any deviations from the standardised protocol will be recorded on the Data Collection Form and will be assessed by the chief researcher.

- Construct and content validity are assured on the basis that the QoR-15 has been extensively validated in many different languages and for many different surgery types.
- Data on the Case Report Forms will be inspected for completeness as per section 4.3.5. Incomplete cases will be excluded from analysis.

- Reliability:
  - The QoR-15 is a reliable tool to use. During development of the tool, the internal consistency was measured using Cronbach α and split-half reliability, both of which had satisfactory results.
  - Reproducibility of the QoR-15 was excellent, and exceeded that reported for the QoR-40, indicating that the QoR-15 score can be interpreted with confidence.

3.9 Bias

Randomisation bias will be avoided by using computer randomisation of patients to either the desflurane or isoflurane groups. The randomisation process will be managed by the statistician who is not involved in patient care. Block randomisation will be done to ensure that an equal number of patients are assigned to each treatment arm.

Selection bias will be reduced by using random block sizes and keeping the chief investigator, research assistant and treating anaesthetists blind to the size of each block.

Response or recall bias is possible with the use of a self-reporting questionnaire. To minimise this, the QoR-15 questionnaire will be administered on Day 1 post-operatively, prior to discharge, which will prevent poor memory recall. Blinding of patients will also help to minimise recall bias. Furthermore, the use of a validated scoring tool that uses clear statements and easy-to-understand scoring, like the QoR-15, should also minimise recall bias.

Observer bias will be limited by the observer who will administer the post-operative questionnaire being blinded to the treatment groups.

The QoR-15 has a score range of 0-150, and it was found not to be limited in its capacity to discriminate patients at the extremes of poor and good recovery. A floor or ceiling effect would therefore be unlikely.

4 Ethics and Dissemination

Informed consent will be taken from all participants by the Chief Researcher. Consent forms will be available in English, Afrikaans and Setswana. Only adult patients who can consent to participation will be included in the study.

A patient information leaflet explaining the objectives of the study in layman's terms has been developed (see Appendix 6.3). This leaflet has been translated into Setswana and Afrikaans. A copy of the patient information leaflet will be given to each patient.

The only document to contain the patient's name will be the sequentially numbered list that will be completed at recruitment. This list will be stored securely by the Chief Researcher. All data will be de-identified: no personal patient information (for example name, date of birth and file number) will be recorded on any study documents (Data Collection Form and QoR-15 forms). Study documents will be numbered sequentially (Data Collection Form and QoR-15 forms for each patient will have the same number). Paper records will be read into the REDCap System in sequence to ensure the study numbers and the electronic record numbers correspond. All paper documents will be stored securely by the Chief Researcher.

Patients will receive the same standard anaesthesia care, irrespective of which group they are randomised to.

Desflurane is registered at the MCC for the maintenance of anaesthesia. Desflurane is freely available in South Africa and will be used for the registered indication in this study.

Permission to perform the study at Dr. George Mukhari Academic Hospital has been obtained from the hospital superintendent. Approval has obtained from the SMU Research Committee, as well as from the SMU Research Ethics Committee. The SMUREC Ethics Reference Number for the study is: SMUREC/M/240/2019:PG. The trial has been submitted for registration with the National Health Research Database (NHRD). A Notification of Phase IV trial was submitted to the South African Health Products Regulatory Authority, with reference number N20210205. The trial has been registered on ClinicalTrials.gov, with reference number NCT04188314.

Any important changes to the protocol after approval (e.g. changes to eligibility criteria, outcomes or analyses) will be communicated to the SMU Research Committee and the SMU Research Ethics Committee.

The results of the trial will be written up by the Chief Researcher for publication in a peer-reviewed academic journal. All supporting documents and de-identified data will be appended as supplements to the main publication. The results will also be presented at the annual SMU Research Day, and at the annual SASA conference, if selected for presentation.

The Chief Researcher holds current certification in Good Clinical Practice. There are no financial or competing interests for the Chief Researcher. There is no industry involvement in this trial.

5 References

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6 Appendices

6.1 SPIRIT Statement Checklist

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Front page
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	2-3
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	4
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	2
	5b	Name and contact information for the trial sponsor	n/a
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	n/a
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-9
	6b	Explanation for choice of comparators	8-9
Objectives	7	Specific objectives or hypotheses	9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	10
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	10-11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11-14
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	n/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	14-16, 23
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	11-14
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	17
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	18-19

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Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	20
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	20
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	20
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	20-21
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	20-21
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	21
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	21
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their *reliability and validity*, if known. Reference to where data collection forms can be found, if not in the protocol	21-22 *25-26*
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	22

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Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	22-23
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	24
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	24
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	n/a
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	25
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	25
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	25
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	27
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	27

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Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	27
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	27
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	27
	31b	Authorship eligibility guidelines and any intended use of professional writers	27
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	27
Appendices			
Informed consent materials	32	Model consent form and *other related documentation given to participants* and authorised surrogates	*34-36* 37-39
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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6.2 Feasibility Questionnaire to Treating Anaesthetists

Feasibility Questionnaire

Date: ___ / ___ / ___

Dear Colleague,

Thank you for taking the time to complete this questionnaire regarding the standardised treatment protocol for my research study comparing the quality of recovery between patients receiving desflurane and isoflurane for maintenance of general anaesthesia. Please refer to the attached document titled "Standardised Anaesthesia Protocol" and answer the questions below.

Do you think the treatment protocol is practical and easy to follow?	Yes	No

Please share any of your thoughts on the practicality of the protocol: _____

Would you feel comfortable giving anaesthesia according to this protocol?	Yes	No

If you answered No, please elaborate: _____

Have you used Desflurane in your clinical practice before?	Yes	No
If you answered **No**, do you feel the protocol explains well enough how to use it?	Yes	No
If you answered **Yes**, would you be happy to use it as per the protocol?	Yes	No

If you have any ideas about the prescribed use of Desflurane, please elaborate: _____

Would you be interested and willing to participate in the study? If yes, please write your name here:

_____

Do you think the protocol covers the management of potential problems well?	Yes	No

Are there any other potential problems you think should be covered in the protocol? _____

Do you have any other concerns about the protocol?	Yes	No

If you answered **Yes**, please elaborate: _____

Overall, do you think the protocol is acceptable?	Yes	No

If you answered **No**, please elaborate: _____

Charlé Steyl; MMed Research; Feb 2020 *DIQoR Trial*

Patient Information Leaflet: Participation in Clinical Trial

Study Name:	A Randomised Control Trial to Compare Quality of Recovery between Desflurane and Isoflurane Inhalational Anaesthesia in Patients Receiving General Anaesthesia for Ophthalmological Surgery at Dr. George Mukhari Academic Hospital (DIQoR Trial)
Chief Investigator:	Dr. Charlé Steyl
Contact Number:	0848000904
Research Assistant:	Tebogo Mabotja
Format of Study:	Randomised, controlled, patient and observer blinded, single-centre superiority trial with two parallel groups.

Dear Sir / Madam,

Thank you for taking part in this research study. This leaflet will give you some background information on how the study will work, and what your role will be.

Background information:

For you to have a safe operation, your eye surgeon has requested that you have general anaesthesia. This means that you will be sleeping and unconscious during your operation.

The doctor that induces this medical sleep is called an anaesthetist. Most often, anaesthetists will inject medicine into your vein to make you fall asleep, and then once you are sleeping, they will keep you asleep with a medical gas that you breathe in.

There are different medical gases available for use. The one that we use most often at Dr. George Mukhari Academic Hospital is called Isoflurane. There is a new gas available called Desflurane, and it may work better than Isoflurane. It is possible with Desflurane that you may wake up faster and feel more awake after your surgery. In this study, we will try to find out if people feel better when they get Desflurane than when they get Isoflurane.

Why is this research being done?

This research study will look at whether people who receive Desflurane during their anaesthesia feel better the day after surgery than people who receive Isoflurane.

Approval for this study has been given by Dr. George Mukhari Academic Hospital, Sefako Magkatho Health Sciences University, and by the Sefako Makgatho University Research Ethics Committee (SMUREC).

Why have I been selected?

This study will be done with healthy adults between the ages of 18-80 years, who are coming for eye surgery. You fit this profile. In total, we will ask 170 patients to be part of our study.

When will this research be done?

This study will take place between February – August 2020.

If I take part in this study, how will it affect my treatment?

If you take part in this study, it will not change any of your other treatment. You will receive the same standard anaesthesia care to make you sleep, to treat any pain you may have and to manage complications like nausea and vomiting. Your surgery will take place exactly as planned by your eye surgeon. The only difference will be in the choice of gas used to keep you asleep during the operation. It is important to understand that both of the gases are safe to use.

Will I know which gas I have been given?

No. In order to get good results, the study is designed so that no one will know which gas they received. If you know which gas was used on you, it may change your answers to our questionnaire!

Can I choose the gas that will be used?

No. In order to get good results, you will not be able to choose which gas your anaesthetist uses. Your anaesthetist will receive a sealed envelope on the day of your surgery, and the gas they have to use will be on a piece of paper inside the envelope. That way there is an equal chance for everyone to receive one or the other of the gases.

What do I need to do?

You will be seen on the day before your surgery by the Chief Investigator of this trial, Dr. Charlé Steyl. She will explain all the information in this leaflet to you and answer any questions you may have. You will then complete a questionnaire that will ask you 15 questions. It takes only 3 minutes to complete. On the morning after your operation, before you are discharged from hospital, the Research Assistant, will come to see you and ask you to complete the same 15-point questionnaire again.

Will any of my personal information be used in this trial?

Your participation in this trial is anonymous; this means that none of your personal identifying information (name, date of birth, hospital file number) will be written on any of the study documents. We will collect certain information like your weight, height, age, gender and details of any medical conditions that you may have, but none of this information can be used to identify you.

What will be done with the results from this study?

The results of the study will be published in an academic journal once it is completed.

If I have more questions, who can I contact?

You may contact Dr. Steyl on 0848000904 if you have any further questions.

6.4 Consent Form

SEFAKO MAKGATHO HEALTH SCIENCES UNIVERSITY ENGLISH CONSENT FORM

Statement concerning participation in a Clinical Trial/Research Project*.

Name of Project / Study / Trial*

A Randomised Control Trial to Compare Quality of Recovery between Desflurane and Isoflurane Inhalational Anaesthesia in Patients Receiving General Anaesthesia for Ophthalmological Surgery at Dr. George Mukhari Academic Hospital *(DIQoR Trial)*

I have read the information on*/ heard the aims and objectives of* the proposed study and was provided the opportunity to ask questions and given adequate time to rethink the issue. The aim and objectives of the study are sufficiently clear to me. I have not been pressurized to participate in any way.

I understand that participation in this Clinical Trial / Study / Project* is completely voluntary and that I may withdraw from it at any time and without supplying reasons. This will have no influence on the regular treatment that holds for my condition, neither will it influence the care that I receive from my regular doctor.

I know that this Trial / Study / Project* has been approved by the Sefako Makgatho University Research Ethics Committee (SMUREC), Sefako Makgatho Health Sciences University and Dr George Mukhari Hospital. I am fully aware that the results of this results of this Trial / Study / Project* will be used for scientific purposes and may be published. I agree to this, provided my privacy is guaranteed.

I hereby give consent to participate in this Trial / Study / Project*.

.....	.....
Name of patient/volunteer	Signature of patient or guardian

.....	.....	.....
Place	Date	Witness

Statement by the Researcher

I provided verbal and/or written* information regarding this Trial / Study / Project*

I agree to answer any future questions concerning the Trial / Study / Project* as best as I am able.

I will adhere to the approved protocol.

Dr. Charle Steyl	.....	.....	Dr. George Mukhari Academic Hospital
Name of Researcher	Signature	Date	Place

*Delete whatever is not applicable.

Standardised Anaesthesia Protocol

Study Name: A Randomised Control Trial to Compare Quality of Recovery between Desflurane and Isoflurane Inhalational Anaesthesia in Patients Receiving General Anaesthesia for Ophthalmological Surgery at Dr. George Mukhari Academic Hospital (DIQoR Trial)

Chief Investigator: Dr. Charlé Steyl

Contact Number: 0848000904

Research Assistant: *To be confirmed*

Format of Study: Randomised, controlled, patient and observer blinded, single-centre superiority trial with two parallel groups.

Dear Colleague,

Thank you for your willingness to participate in this research study. This document explains how the anaesthesia care will be standardised for patients in this study.

Patient Selection:

Patients will be selected and recruited on the day before surgery by the Chief Investigator. Informed consent for study participation will be taken. Demographic information will be completed on the Case Report Form. Healthy (ASA I & II) adult patients between the ages of 18-80 years, booked for ophthalmological surgery will be considered for inclusion in the trial.

Randomisation:

Patients will be randomly allocated to either the Isoflurane group (control) or the Desflurane group (intervention). On the day of the surgery, you will receive a sealed opaque envelope with the group that the patient falls into. Please follow the instructions below according to the agent to be used. Please attach the randomisation slip to the Case Report Form.

Pre-Medication:

Patients will not receive any pre-medication.

Induction of Anaesthesia:

1. Fentanyl 3 mcg/kg pre-induction
2. Lignocaine 40 mg pre-induction to minimize Propofol-induced injection pain
3. Propofol 2 mg/kg until induction of anaesthesia
4. Dexamethasone 8mg after induction of anaesthesia to prevent post-operative nausea and vomiting and to reduce opioid consumption.
5. Mask ventilation with 6 l/min 100% oxygen until airway is placed
6. Airway management will be with a Laryngeal Mask Airway (LMA), size selected according to patient weight.

Isoflurane Group: Maintenance of Anaesthesia:

1. Once the airway is secured, reduce fresh gas flow to 2 l/min.
2. Open the Isoflurane vaporiser and adjust to attain 1MAC.
3. Once 1MAC is attained, reduce fresh gas flow to 0.2 l/min 100% oxygen.
4. Adjust the vaporiser to maintain 1MAC throughout the procedure.
5. The use of basal fresh gas flow is intentional to minimise vapour used. When basal flow is used, 100% oxygen is required to meet oxygen demand.

Desflurane Group: Maintenance of Anaesthesia:

1. Once the airway is secured, reduce fresh gas flow to 2 l/min.
2. Open the Desflurane vaporiser to 12%.
3. Maintain these settings until 1MAC is reached, about 3 minutes.
4. Now reduce the fresh gas flow to 0.2 l/min 100% oxygen.
5. Adjust the vaporiser to maintain 1MAC throughout the procedure.
6. The use of basal fresh gas flow is intentional to minimise vapour used. When basal flow is used, 100% oxygen is required to meet oxygen demand.

Wash-out of Volatile Anaesthetic:

1. At the end of the procedure, close the vaporiser.
2. Increase fresh gas flow to 6 l/min.
3. Remove the Laryngeal Mask Airway when clinically appropriate.

Managing Potential Problems:

1. Should the bag on the anaesthetic machine collapse during basal flow anaesthesia (e.g. because of a poor seal from the LMA, the bag may be re-inflated by pushing the Oxygen Flush button. Vapour flow should be adjusted to maintain 1MAC.
2. Should the ophthalmologist complain that the patient is in too light a plane of anaesthesia, the patient may be deepened with a bolus of Propofol 0.5-1 mg/kg.
3. For intra-operative analgesia (for example if patient develops tachycardia or hypertension), administer 50mcg Fentanyl boluses intravenously.
4. For post-operative analgesia in recovery (only if required), administer Tramadol 50-100mg intravenously as a bolus.
5. For post-operative nausea (only if required), administer Ondansetron 4mg intravenously as a bolus, followed by Metoclopramide 10mg intravenously after 30 minutes (only if required).

Recording Data on the Case Report Form:

- Please ensure that you complete all the required fields on the Case Report Form.
- Please record any additional medication given to the patient as per above protocol to manage problems like post-operative pain or nausea.
- Please record adverse events on the Case Report Form and inform Dr. Steyl immediately.
- In the unlikely event of Malignant Hyperthermia, please stop all volatiles and follow emergency management protocols.
- Please hand the Case Report Form to Dr. Steyl at the end of the procedure.

Standardised Anaesthesia Protocol (Version 2)

Study Name: A Randomised Control Trial to Compare Quality of Recovery between Desflurane and Isoflurane Inhalational Anaesthesia in Patients Receiving General Anaesthesia for Ophthalmological Surgery at Dr. George Mukhari Academic Hospital (DIQoR Trial)

Chief Investigator: Dr. Charlé Steyl

Contact Number: 0848000904

Research Assistant: Tebogo Mabotja

Format of Study: Randomised, controlled, patient and observer blinded, single-centre superiority trial with two parallel groups.

Dear Colleague,

Thank you for your willingness to participate in this research study. This document explains how the anaesthesia care will be standardised for patients in this study.

Patient Selection:

Patients will be selected and recruited on the day before surgery by the Chief Investigator. Informed consent for study participation will be taken. Demographic information will be completed on the Case Report Form. Healthy (ASA I & II) adult patients between the ages of 18-80 years, booked for ophthalmological surgery will be considered for inclusion in the trial.

Randomisation:

Patients will be randomly allocated to either the Isoflurane group (control) or the Desflurane group (intervention). On the day of the surgery, you will receive a sealed opaque envelope with the group that the patient falls into. Please follow the instructions below according to the agent to be used. Please attach the randomisation slip to the Case Report Form.

Machine Check and Leak Test:

Please make sure that the machine is tested daily, with a new, clean circuit. Please record the machine leak on the case report form. Ensure that the CO2 absorber (sodalime) is checked daily and replaced when needed.

Pre-Medication:

Patients will not receive any pre-medication.

Induction of Anaesthesia:

1. Fentanyl 1.5-3 mcg/kg pre-induction (about 100-200 mcg for most adults). Use the lower dose for short procedures and the larger dose for longer procedures.
2. Lignocaine 40 mg pre-induction to minimize Propofol-induced injection pain.
3. Propofol 2-2.5 mg/kg until induction of anaesthesia (150-200mg for most adults).
4. Dexamethasone 8mg after induction of anaesthesia to prevent post-operative nausea and vomiting and to reduce opioid consumption.
5. Mask ventilation with 6 l/min 100% oxygen until airway is placed.
6. Airway management with a Laryngeal Mask Airway (LMA), size selected according to patient weight.

Use of Muscle Relaxants During Procedure:

If required, a small dose of muscle relaxant may be administered to facilitate immobility during the procedure. For Rocuronium, a dose of up to 0.15mg/kg may be used (about 10-15mg for most adults). For Cisatracurium, a dose of up to 0,05mg/kg may be used (about 2.5 – 4mg for most adults). Top-up doses may be given every 30-40 minutes, if required; dosing should be the same as the initial dose. Ensure reversal of the muscle relaxant with Neostigmine 10-20 minutes before the end of the procedure.

Isoflurane Group: Maintenance of Anaesthesia:

1. Once the airway is secured, reduce fresh gas flow to 2 l/min.
2. Open the Isoflurane vaporiser and adjust to attain 1MAC.
3. Once 1MAC is attained, reduce fresh gas flow to 0.2-0.5 l/min. Aim to reduce the fresh gas flow as low as possible, taking into consideration the machine leak.
4. Adjust the vaporiser to maintain 1MAC throughout the procedure.
5. If basal flow (0.2L/min) is reached, ensure that FiO2 is 100% to meet the patient's oxygen demand.
6. Should the bellows on the anaesthetic machine collapse during basal or minimal flow anaesthesia, take the following steps: Increase the FGF to 2 l/min and adjust the vaporiser concentration to maintain 1MAC. Continue like this until the bellows are filled, then return to the previous setting in concentration and FGF.

Desflurane Group: Maintenance of Anaesthesia:

1. Once the airway is secured, reduce fresh gas flow to 2 l/min.
2. Open the Desflurane vaporiser to 12%.
3. Maintain these settings until 1MAC is reached, about 3-5 minutes.
4. Once 1MAC is attained, reduce fresh gas flow to 0.2-0.5 l/min. Aim to reduce the fresh gas flow as low as possible, taking into consideration the machine leak.
5. Slowly adjust the vaporiser concentration to maintain 1MAC throughout the procedure (usually 8-10%).
6. If basal flow (0.2L/min) is reached, ensure that FiO2 is 100% to meet the patient's oxygen demand.
7. Should the bellows on the anaesthetic machine collapse during basal flow or minimal flow anaesthesia, take the following steps: Turn the vaporiser concentration back to 12%, then increase the FGF to 2 l/min. Continue like this until the bellows are filled, then return to the previous setting in concentration and FGF.

End of Procedure:

1. If a small dose of muscle relaxant was used, ensure that it is fully reversed with Neostigmine 0.04mg/kg (2-3mg for most adults) 10-20 minutes before the end of the procedure. Glycopyrrolate or Atropine may be added to prevent bradycardia and gastro-intestinal side-effects.
2. At the end of the procedure, close the vaporiser and increase fresh gas flow to 6 l/min.
3. Remove the Laryngeal Mask Airway when clinically appropriate.

Managing Potential Problems:

1. Should the ophthalmologist complain that the patient is in too light a plane of anaesthesia, the patient may be deepened with a bolus of Propofol 0.5-1 mg/kg.
2. For intra-operative analgesia (for example if patient develops tachycardia or hypertension), administer 50-100 mcg Fentanyl boluses intravenously, as needed.
3. In cases where post-operative pain is anticipated, administer Tramadol 50-100mg intravenously as a bolus about 20 minutes before the end of the procedure.
4. For post-operative nausea (only if required), administer Ondansetron 4mg intravenously as a bolus, followed by Metoclopramide 10mg intravenously after 30 minutes (only if required).

Recording Data on the Case Report Form:

- Please ensure that you complete all the required fields on the Case Report Form.
- Please record any additional medication given to the patient as per above protocol to manage problems like post-operative pain or nausea.
- Please record adverse events on the Case Report Form and inform Dr. Steyl immediately.
- In the unlikely event of Malignant Hyperthermia, please stop all volatiles and follow emergency management protocols.
- Please hand the Case Report Form to Dr. Steyl at the end of the procedure, or place in the box in recovery room.
- The rest of the documents (consent form, quality of recovery forms) should remain in the patient's file.

6.7 Case Report Form: Data Collection

Case Report Form: Data Collection

Date: ___ / ___ / ___ Study #: _____

SECTION A: PATIENT INFORMATION:

Age: _____ years

Gender: | Male | Female |

Weight: _____ kg **Height:** _____ m **BMI:** _____

ASA Status: | I | II | III | IV | V |

Risk for PONV: | Female | Previous PONV | Motion Sickness | Non-smoker |

Smoking History: | Non-smoker | Ex-smoker | Current Smoker | **Pack years:** _____

Comorbidities:

None	Hypertension	Diabetes	Pulmonary Disease	Cardiovascular Disease
Cerebrovascular Disease	Renal Disease	HIV	Psychiatric Conditions	Other *(Specify below)*

If Other, Details of Condition: _____

Any Anaesthesia in the Past Month? | Yes | No |

If YES: | General | Regional | Local Infiltration |

Any Complications? | Yes | No |

If YES, Describe: _____

SECTION B: INFORMATION ABOUT PROCEDURE:

Group: | Desflurane | Isoflurane |

Intravenous Induction Time: _____ **End of Anaesthesia:** _____

Time Vapour Started: _____ **Time Vapour Stopped:** _____

Millilitres of Vapour Used: _____ ml **Machine Leak Amount:** _____ ml

Propofol at Induction: _____ mg **FGF used most of time:** _____ ml/min

Fentanyl at Induction: _____ mcg **Muscle Relaxant:** | Rocuronium | Cisatracurium | _____ mg

Intra-op Propofol Top-up:	No	Yes →	Number of top-ups given: _____	Total top-up dose: _____ mg
Intra-op Fentanyl Top-up:	No	Yes →	Number of top-ups given: _____	Total top-up dose: _____ mcg
Intra-op Muscle Relax. Top-up:	No	Yes →	Number of top-ups given: _____	Total top-up dose: _____ mg
Neostigmine given:	No	Yes →	Time: _____	Dose: _____ mg
Atropine / Glycopyrrolate given:	No	Yes →	Time: _____	Dose: _____ mg
Intra- or Post-op Tramadol:	No	Yes →	Time: _____	Dose: _____ mg
Post-Op Ondansetron:	No	Yes →	Time: _____	Dose: _____ mg
Post-Op Metoclopramide:	No	Yes →	Time: _____	Dose: _____ mg

Adverse events: | Bronchospasm | Laryngospasm | Nausea / Vomiting | Other *(specify below)*

Please inform Dr. Steyl immediately of any adverse events (0848000904)

Time into Recovery: _____ **Time out of Recovery:** _____

Anaesthesia administered as per study protocol: | Yes | No |

If no, please describe modification: _____

Charlé Steyl; MMed Research; Feb 2020 *DIQoR Trial*

6.8 Case Report Form: QoR-15 English

QoR-15 Patient Survey

Date: ___ / ___ / ___ Study #: _____

Pre-Operative ☐ Post-Operative Day 0 ☐ Post-Operative Day 1 ☐

PART A

How have you been feeling in the last 24 hours?

(0 to 10, where 0 = none of the time [poor] and 10 = all of the time [excellent])

1.	Able to breathe easily	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
2.	Been able to enjoy food	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
3.	Feeling rested	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
4.	Have had a good sleep	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
5.	Able to look after personal toilet and hygiene unaided	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
6.	Able to communicate with family or friends	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
7.	Getting support from hospital doctors and nurses	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
8.	Able to return to work or usual home activities	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
9.	Feeling comfortable and in control	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
10.	Having a feeling of general well-being	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time

PART B

Have you had any of the following in the last 24 hours?

(10 to 0, where 10 = none of the time [excellent] and 0 = all of the time [poor])

1.	Moderate pain	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
2.	Severe pain	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
3.	Nausea or vomiting	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
4.	Feeling worried or anxious	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
5.	Feeling sad or depressed	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time