MAIN DISSERTATION

University of Cape Town

REASONS FOR POOR OR BORDERLINE CATARACT SURGICAL OUTCOMES AT NKHOMA HOSPITAL IN MALAWI: A RETROSPECTIVE ANALYSIS

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DECLARATION

I, **Martha Chingwengwe** certify that this is my own work which has never been presented before or concurrently being presented in any institution for award of any degree**.**

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Date: 31st January 2024

SECTIONS / PARTS

PART A: This part presents protocol of research study approved by Faculty of Health Sciences Human Research Ethics Committee at University of Cape Town, South Africa and the National Health Sciences Research Committee in Malawi. In addition, the part comprises of a structured literature review.

PART B: PLOS ONE journal manuscript comprising of introduction, methods section, results section and discussion section.

PART C: Comprised of supplementary documents, including acknowledgements, data capture forms, ethical approvals and PLOS ONE journal author instructions.

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ACRONYMS

BCVA	Best Corrected Visual Acuity
CHAM	Christian Health Association of Malawi
CSC	Cataract Surgical Coverage
CSR	Cataract Surgical Rate
EVI	Early Visual Impairment
IOL	Intra Ocular Lens
LMIC	Low- and Middle-Income Countries
MVI	Moderate Visual Impairment
NEP	Nkhoma Eye Programme
NGO	Non-Governmental Organisation
RAAB	Rapid Assessment of Avoidable Blindness
SSA	Sub Saharan Africa
VA	Visual Acuity
VLEG	Visual Loss Expert Group
WHO	World Health Organisation

PART A: PROTOCOL

REASONS FOR POOR OR BORDERLINE CATARACT SURGICAL OUTCOMES AT NKHOMA HOSPITAL, MALAWI: A RETROSPECTIVE ANALYSIS

INTRODUCTION

Poor or borderline outcomes of cataract surgery, if not managed effectively, are indications of poor-quality cataract surgical services. Cataract, a leading cause of global blindness, affects 253 million people worldwide, with 89% residing in low- and middle-income countries and 55% being women (Bourne, et al., 2017). Cataract is responsible for a substantial portion of blindness in sub-Saharan Africa, including Malawi, emphasizing the need for high quality cataract surgical services.

Recognizing cataract blindness as both avoidable and treatable, cataract surgery, which involves the removal of the opacified crystalline lens and the insertion of a synthetic intraocular lens, is a cost-efficient and effective intervention (Baltussen et al., 2004). Accessible, high-quality surgical services are crucial in addressing vision loss due to cataract. However, the efficiency and effectiveness of cataract services directly impact visual outcomes after surgery, necessitating a focus on achieving positive results.

While generally favourable outcomes are obtained in developed countries, visual acuity following cataract surgery vary globally, especially in low- and middle-income countries where the percentage of patients with poor visual outcomes is below World Health Organisation (WHO) standards (WHO, 2019). The WHO categorizes outcomes as good, borderline, or poor based on Best Corrected Visual Acuity (BCVA) (WHO, 1998). The World Health Organization (WHO) recommends that a minimum of 80% of operated eyes should exhibit good post-operative outcomes, with no more than 5% categorized as poor outcomes (WHO, 2015), see below:

- Good outcome: VA after surgery is 6/18 or better,
- Borderline outcome: VA after surgery is < 6/18 to 6/60, and
- Poor outcome: VA after surgery is worse than 6/60 (<6/60 to no light perception).

This classification system serves as a benchmark for evaluating the success of cataract surgical services whether optimal or suboptimal.

In Malawi, Nkhoma Hospital is a leading cataract surgical facility, contributing significantly to the country's surgical output. Affiliated with the Christian Health Association of Malawi (CHAM), Nkhoma Hospital initiated the Nkhoma Eye Programme (NEP) in 2000, striving to eliminate avoidable blindness

and visual impairment due to cataract in the country. Over the last two decades, NEP, in collaboration with national and international partners, has played a pivotal role in providing eye care services in central Malawi. Notably, the hospital's improved cataract surgical output is attributed to infrastructure development and increased support from various stakeholders.

RATIONALE OF THE STUDY

Strengthening cataract surgical services is integral to reducing blindness and visual impairment, and a key aspect involves enhancing the quality of cataract surgery outcomes. While the NEP is recognized for its leadership in high-volume cataract surgeries, a crucial aspect, the quality of surgical outcomes, has not been systematically assessed at the programme level. The sheer volume of surgeries alone may not contribute optimally to sight restoration if the quality is suboptimal. Therefore, a focused examination of the quality of surgical outcomes is imperative.

At Nkhoma Hospital, cataract surgeries have been performed by ophthalmologists and cataract surgeons using a suture-less technique since 2004 (Dean et al., 2014). Over the past two decades, continuous improvements in surgical techniques and an increased number of surgeons have positively impacted surgical outcomes at Nkhoma Hospital (Dean et al., 2014). The hospital's eye department produces routine quality management reports as part of a funding agreement with an international NGO, contributing to ongoing monitoring and improvement efforts.

Despite the high surgical volume, there is a lack of objectively verified data on the quality of cataract surgical outcomes. Understanding the reasons behind poor or borderline outcomes at a high-volume facility like Nkhoma Hospital is crucial for implementing timely corrective measures.

Limited studies in low- and middle-income countries (LMICs) have focused on the quality of cataract surgery outcomes. Some studies suggest that cataract patients are more likely to seek surgical help when assured of a positive outcome (Lewallen et al., 2015). Other studies indicate a willingness to pay for services of good quality (Dean, 2012). Unravelling the reasons for suboptimal cataract surgery outcomes at Nkhoma Hospital is vital for addressing potential barriers and improving overall surgical quality.

Main objective

The primary aim of this study is to identify the reasons for poor or borderline cataract surgical outcomes at Nkhoma Hospital, Malawi, specifically focusing on patients who underwent surgeries between January and December 2019.

Subsidiary objectives

1. To describe the association between age, gender and the reasons for poor or borderline surgical outcomes at Nkhoma Hospital.
2. To assess the association between the type of surgeon conducting surgery and the reasons for poor or borderline quality of cataract surgery.
3. To assess the association between route / mechanism of referral of patients for cataract surgery and the reasons for poor or borderline quality of cataract surgery.at Nkhoma Hospital
4. To explore the most common cataract surgical complications at Nkhoma Hospital.

The outcomes of this research will provide crucial information about the quality of cataract surgical services for Nkhoma Hospital's leadership and other stakeholders in Malawi and the broader region. By understanding and addressing the identified factors, strategies can be developed to improve the quality of cataract surgery outcomes. This, in turn, will contribute to the reduction of blindness and visual impairment caused by cataracts in Malawi. Furthermore, the study's findings will contribute to the knowledge base of eye hospitals in Malawi and beyond.

The Government of Malawi, along with other non-governmental organizations (NGOs), can leverage the insights gained from this study to formulate informed policies aimed at eliminating cataract-induced blindness and visual impairment in the country. Overall, this research aims to make a meaningful impact on the field of cataract surgery, ultimately improving the well-being of patients in Malawi and contributing to global efforts in eradicating preventable blindness.

LITERATURE REVIEW

Prevalence of blindness

Globally, cataract is the most common cause of blindness and the second major contributor to visual impairment (Bourne et al., 2017). In 2015, the Vision Loss Expert Group (VLEG) reported 253

million blind or visually impaired individuals, with 89% residing in low- and middle-income countries (LMICs) (Flaxman et al., 2017). Cataract remains the leading cause of treatable blindness worldwide.

Over the past two decades, there has been a significant reduction in the prevalence of vision loss. According to the VLEG/Global Burden of Disease 2020 model, the global prevalence of blindness and visual impairment decreased from 1999 estimates, with 43.2 million people blind and 295 million severely visually impaired in 2019 (IAPB Vision Atlas, 2020). This positive trend is attributed to improved statistical analysis and the inclusion of precise data from various Rapid Assessment of Avoidable Blindness (RAABs) surveys conducted in different regions.

Despite global improvements, regional disparities persist, with LMICs in South Asia and Sub-Saharan Africa experiencing the highest rates of vision loss. In Sub-Saharan Africa, cataract accounts for 35-45% of blindness and 25-35% of visual impairment (Flaxman et al., 2017). Limited primary healthcare measures, low staffing levels, inadequate infrastructure, and scarce community programmes contribute to the high prevalence in these regions.

Malawi, specifically, has one of the highest rates of cataract-induced blindness in Sub-Saharan Africa, with 1% of the population being blind (Dean et al., 2014). RAAB findings in Malawi, Zambia (Lindfield, 2012) and Zimbabwe (Minnies, 2019) support these claims, with the main causes of blindness in Malawi being cataract, trachoma, glaucoma, and Vitamin A deficiencies.

Blindness/visual loss versus age and sex

Recent studies indicate a correlation between vision loss, age, and gender across regions, countries, and communities. A VLEG systematic review revealed that increasing age is associated with a higher risk of vision loss, with 73% of people aged 50 and above at risk (Bourne et al., 2020). The study also noted that 53% of people with vision loss are women and girls, emphasizing the importance of improving accessibility to cataract surgery services for women.

RAAB survey data in the Southern African region show age- and sex-adjusted prevalence of blindness in people aged 50 and above ranging from 1.9% to 4.1%, corroborated by various researchers in the region (Minnies, 2022; Mutati, 2017; RAAB-World, 2022).

Indicators of cataract services

Two key indicators assess cataract service availability and accessibility: Cataract Surgical Rate (CSR) and Cataract Surgical Coverage (CSC). Data obtained from RAABs provide information on cataract surgical coverage and outcomes.

CSR measures the effectiveness of eye services in providing care, calculated as the total number of cataract operations per million population over a one-year period in a country, district, or region (Wang et al., 2017). LMICs generally exhibit lower CSRs compared to high-income countries. For instance, in 2019, Malawi reported a CSR of 268, ranking 159th out of 176 countries (IAPB, 2022), indicating a lag in cataract services that hinders the elimination of blindness due to treatable causes.

CSC gauges the extent to which individuals with cataract-related vision loss have undergone surgery, serving as an indicator for the adequacy, availability, accessibility, and affordability of cataract surgical services (Wang et al., 2017). In 2010, Malawi had a CSC of 13.9% (IAPB Vision Atlas, 2022), highlighting issues of inaccessibility, unaffordability and inadequacy in cataract services.

In the 2019 World Report on Vision, the WHO reaffirmed cataract as the leading cause of blindness globally, emphasizing the need to maintain high-quality cataract surgical services (Dean et al., 2012). Monitoring surgical outcomes is vital for assessing quality, as poor outcomes reduce the effectiveness and efficiency of eye care programs. For instance, patients may experience symptoms like watering, blurred vision and red eyes after cataract surgery, contributing to reluctance to undergo the procedure.

Overall, as efforts are made to meet cataract surgical service targets, emphasis should also be placed on ensuring high-quality outcomes, ultimately contributing to global endeavours in eliminating preventable blindness.

Barriers to the uptake of cataract surgery

According to a systematic review, the main barriers to cataract surgery in Africa are low awareness, accessibility, and acceptance of cataract services (Aboobaker & Courtright, 2016). These barriers can be overcome by implementing known strategies.

Table' 1: Barriers to uptake of surgery and strategies to overcome them. Author synthesis (2022)

Barrier	Example	Strategies to overcome
Unaffordability	High cost of surgery and indirect costs like transport & opportunity cost	Provide free services, transport and do surgical outreach camps
Cultural & socio-economic	Gender-based inequities, cultural beliefs, poverty, time, and opportunity	Provide health education, raise awareness, target vulnerable groups like women and disabled.
Knowledge	Limited information of facilities, eye conditions	Conduct regular health promotion campaigns in local languages.
Fear of surgery outcome	Lack of understanding of the surgical process; history of poor outcomes.	Make use of pseudophakic motivators, monitor and improve cataract surgical outcomes.
Seeing no reason for surgery (No need)	Acceptance of the condition	Conduct health promotion, community empowerment programmes.
Accessibility	Distance to/from surgical centre	Bring cataract services near to people and increase frequency of service

A hospital-based cross-sectional study conducted in Malawi (Dean et al., 2012) revealed that the average monetary amount cataract patients were willing to pay for surgery was below the actual cost, which includes screening, transport, accommodation and the surgical procedure itself. Notably, data from various sources, including a study in Tanzania (Geneau et al., 2005) and another in Mozambique (Roba et al., 2020), consistently highlight gender-based disparities in cataract surgery uptake. Women, despite having slightly higher cataract rates than men, are significantly less likely to undergo surgery. Reasons for this include women not expressing their need for better sight as strongly as men and fearing the perception of being a burden. Addressing these disparities requires decentralizing knowledge about cataract services to community health facilities, integrating traditional health systems with conventional ones to dispel myths and improve awareness (Khoza et al., 2017).

In Mozambique, (Roba, et al., 2020) underscored inadequate knowledge on cataract services, with 34.9% of women and 26.3% of men unaware of the treatability of cataracts. This underscores the

need for widespread education to overcome myths associated with cataracts. Patient satisfaction and positive surgical outcomes play a crucial role in motivating others to undergo cataract surgery, while fear of poor outcomes can deter potential patients (Aboobaker & Courtright, 2016). Despite the potential underreporting in Rapid Assessment of Avoidable Blindness (RAAB) surveys, consistently high-quality cataract surgery is imperative for building trust in cataract service programs.

Factors contributing to poor surgery outcomes, such as surgeon experience, equipment quality, and the presence of co-morbidities (Bourne et al., 2020), can be mitigated through enhanced case finding, effective screening and referral practices, refractive error correction and staff training. Without addressing these factors, the effectiveness of cataract services remains uncertain. While cataract surgery aims to restore vision and enhance the quality of life for the blind or visually impaired, optimal outcomes are often elusive, particularly in Africa and Asia (Bourne et al., 2020). The existing emphasis on quantitative targets may overshadow the need for quality outcomes.

Monitoring cataract surgery outcomes is crucial for assessing and enhancing the quality and effectiveness of cataract surgical services. Post-cataract surgery visual acuity (VA) serves as an indicator for ophthalmologists and cataract surgeons to evaluate service quality. Assessment, with best correction (pinhole) or available correction (patients' own spectacles or functioning vision), should occur within 24 hours and/or 6-8 weeks post-operation. The World Health Organization (WHO) recommends that a minimum of 80% of operated eyes should exhibit good post-operative outcomes, with no more than 5% categorized as poor outcomes (WHO, 2015), see below:

- Good outcome: VA after surgery is 6/18 or better,
- Borderline outcome: VA after surgery is < 6/18 to 6/60, and
- Poor outcome: VA after surgery is worse than 6/60 (<6/60 to no light perception).

This classification system serves as a benchmark for evaluating the success of cataract surgical services.

Reasons for poor or borderline cataract surgery outcomes

RAAB surveys have consistently identified ocular co-morbidity, surgical complications, uncorrected refractive error and long-term complications as the primary reasons for poor and borderline

outcomes in cataract surgery (Lavy et al., 2007). In the Southern Region of Malawi, the report of the 2010 RAAB survey revealed that 35.9% of cataract surgery outcomes were classified as poor, with key reasons cited as "comorbidity" (40%), "surgery complication" (46.7%), and "sequelae" (13.3%) (Kalua, 2010).

Patient selection and comorbidities

Effective patient selection is crucial to avoid poor outcomes, particularly in cases of comorbidities such as chronic glaucoma, age-related macular degeneration, and diabetic retinopathy. Lindfield et al. (Lindfield, et al., 2012) emphasize the need to exclude patients with significant other pathologies, as their presence is likely to result in suboptimal outcomes post-cataract surgery. A prospective study in Ethiopia (Marko, et al., 2020) further supports this by suggesting that optimizing patient selection can significantly improve cataract surgery outcomes, especially in patients with pre-existing co-morbidities.

Intraoperative complications and post-operative care

Surgery with intraoperative complications can lead to poor outcomes, including low visual acuity, discomfort, bruising, swelling of the eyelid, increased intraocular pressure and allergic reactions to administered medications (Miller et al., 2016). Early and late complications, such as persistent inflammation and posterior capsule opacification, contribute to unfavourable outcomes. Post-operative care and vigilant monitoring by surgeons play a crucial role in early detection and management of complications, ultimately influencing overall surgical success (Dean et al., 2014).

Strategies to improve cataract surgical outcomes

To enhance outcomes, a comprehensive pre-operative examination is essential for excluding significant other pathologies, such as advanced glaucoma or other causes of lens opacity, which are common misdiagnoses in African patients (Jolley & Cumaio, 2020). Surgeons must undergo adequate supervised training and be equipped with the necessary instruments and consumables. Continuous monitoring of surgical outcomes, as suggested (Lindfield, et al., 2012) enables surgeons to identify areas for improvement and refine their techniques.

Transition to IOL implantation

The transition from intra-capsular cataract extraction with aphakic spectacle correction to extracapsular cataract extraction with intraocular lens (IOL) implantation has significantly contributed to improved outcomes (Lindfield et al., 2012). Recent RAAB surveys in the Sub-Saharan region report over 95% IOL insertion rates (RAAB World, 2022). Post-operative follow-up, as recommended (Dean, et al., 2014), ensures the early detection and treatment of complications, further enhancing overall surgical success.

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PART B: JOURNAL MANUSCRIPT - PLOS ONE

Reasons for poor or borderline cataract surgical outcomes at Nkhoma Hospital, Malawi: a retrospective analysis

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Abstract

Cataract is the main cause of blindness worldwide. Cataract surgery is the most effective intervention for cataract blindness. However, poor or borderline outcomes following cataract surgery reduces the effectiveness of this strategy to eliminate this cause of avoidable blindness. This study aimed to determine the reasons for poor or borderline cataract surgical outcomes in people who had undergone cataract surgery at Nkhoma Hospital in Malawi from January to December 2019.

This was a retrospective analysis of theatre records of people who had undergone cataract surgery at Nkhoma Hospital between January and December 2019. All people that recorded a post-operative visual acuity of 6/18 and worse in either or both eyes were included in the study. Data was collected on variables concerning demographics, aspects of referral, preoperative examination, intraoperative findings and post- operative examination.

The study determined that 52.2% of poor or borderline cataract surgical outcomes at Nkhoma Hospital were because of ocular comorbidity known to cause vision loss and other comorbidity likely to affect vision adversely, 25.8% because of uncorrected refractive error (post-operative visual acuity with pinhole improved to 6/18 or better) and 3.7% because of intra-operative complications. For a total of 13.5% of the poor and borderline surgery outcome cases, no reasons could be determined with the data available.

The study revealed that the reasons for poor or borderline surgery outcome at Nkhoma Hospital are complex and are influenced by decision-making about whether to perform the surgery, regardless of pre-operative visual acuity findings, presence of co-morbidities or the reasonable expectation to deliver an improved outcome following surgery. This emphasizes the need or improved knowledge and skills about referrals, pre-operative screening, post-operative follow-up and allocation of workloads to members of the entire cataract surgical service team.

Introduction

Poor or borderline outcomes are suboptimal results in cataract surgery. Cataract surgery outcomes indicates the quality of cataract surgical services. If not well managed, poor or borderline outcomes may result in impaired vision. This is significant as cataract is the leading cause of blindness globally.

Visual outcomes from cataract surgery vary between and within countries.[1] Generally, cataract surgery results in good outcomes in developed countries leading to improved vision of patients. However, in most low- and middle-income countries (LMICs) the percentage of people with poor visual outcomes after cataract surgery is higher than the WHO standard.[2] The assessment of cataract surgery outcomes is a necessary step towards improving cataract surgery quality in developing countries including Malawi.

Rationale of the study

At Nkhoma Hospital in Malawi, an ophthalmologist and two cataract surgeons perform cataract surgeries, using a suture-less technique.[3] For the past two decades, there has been improvement in the surgery techniques as a result of various training and increased number of surgeons, and this has resulted in the improvement of surgical outcome at Nkhoma Hospital.[3] The Nkhoma Hospital Eye Care Programme produces routine quality management reports as part of a funding agreement with an international NGO.[3]

While the Nkhoma Hospital Eye Care Programme has been labelled as a leader in high volume cataract surgeries, the quality of surgical outcomes has never been assessed. A programme may perform many surgeries but if the quality is poor, the rate of sight restoration may not contribute maximally to the reduction of blindness and visual impairment in the target population (Dean, et al., 2014). More attention should be given to examine the quality of surgery outcomes.

There have been few studies that focused on the quality of the surgical outcome of cataract surgical outcomes in LMICs. Some studies have shown that people with cataract are more likely to

seek surgical help when they are almost certain that the outcome will be good.[4] Other studies indicated that people are willing to pay if high quality services are available.[5] Hence, it is very important to understand the reasons for poor or borderline cataract surgery outcomes in LMICS.

Over the years, various Rapid Assessment of Avoidable Blindness (RAAB) surveys have identified the main reasons for poor or border-line outcomes of cataract surgery. These are as ocular co-morbidity (Selection), surgical complications (Surgery), uncorrected refractive error (Spectacles) or long-term complications (Sequelae).[6] In 2010, the Southern Malawi RAAB survey reported that 35.9 percent (%) of the cataract surgery outcome were poor.[7] Reasons for poor or borderline outcomes were cited as "comorbidity 40%", "surgery complications 46.7%" and "sequelae 13.3%".

The selection of people to undergo cataract surgery has to be done with careful consideration as to whether to exclude people with co-morbidities such as chronic glaucoma, age-related macular degeneration and diabetic retinopathy. This is because outcome in eyes with significant other pathology is likely to result in a poor outcome following cataract surgery, despite successful lens extraction and intraocular lens insertion.[1] This is a decision to be made by an experienced and competent cataract surgeon (K. Kalua 2024, expert opinion, 17 January). A prospective, longitudinal study on adult people scheduled for cataract surgery between 2018 and 2019 in Ethiopia found that optimizing patient's selection could improve cataract surgery outcomes in people with pre-existing co-morbidities by 80%.[8]

Surgery with intraoperative complications is likely to result in a poor outcome.[1] Some of these complications can involve discomfort or pain, bruising and swelling of the eyelid, increased intraocular pressure, and allergic reaction to the medicines administered.[9] These complications may present post-operatively or much later, during follow-up.

In the past two decades, there has been significant decline in the prevalence of vison impairment, thanks to the Vision 2020 strategy (IAPB, 2020). According to the Vision Loss Expert Group /

Global Burden of Disease 2020 analysis, the prevalence of blindness and visual impairment decreased from projections of 75 million in 1999, to a total of 43.2 million people blind and 295 million severely visually impaired in 2019 globally.[10] This improvement has been attributed to improved statistical analysis and inclusion of up-to-date data generated from RAAB surveys conducted in various regions, as well as the increase in availability of eye care services.

Despite the improvements at global level, there are regional inequalities. Low- and middle-income countries, especially in South Asia and Sub-Saharan Africa are experiencing the highest rates of vision loss.[11] Malawi has one of the highest rates of blindness in Sub-Saharan Africa with 1% of the population being blind and 51% due to cataract.[3]

It is important to ensure that quality of cataract surgical services is high.[5] Monitoring cataract surgery outcomes is an important practice that provides information that can aid the improvement of the quality of cataract surgery.[12] This in turn can lead to improved effectiveness and efficiency of cataract surgical services. Poor quality of surgical outcomes reduces the effectiveness and efficiency of an eye care programme, because people must undergo repeated surgery and services must deal with other symptoms of poor outcomes.[1] For example, watering and blurred vision. These can contribute to people's reluctance to undergo cataract surgery.

Poor surgery outcomes are usually attributed to factors such as surgeon's experience, the equipment and materials used during the surgery and the presence of co-morbidities.[11] These factors can be addressed through improved case finding, effective screening and referral practices, refractive error correction and training of staff. If cataract surgical outcomes are poor, then effectiveness of the cataract services cannot be guaranteed.

It is important to know the reasons for poor or borderline quality of cataract surgery outcomes at a high-volume surgical facility like Nkhoma Hospital. The aim of this study is to examine the

outcomes of cataract surgeries conducted between 1 January and 31 December 2019 and identify the reasons for poor or borderline surgical outcomes.

Primary objective

The primary objective of the study was to determine reasons for poor or borderline cataract surgical outcomes at Nkhoma Hospital, Malawi. In patients that had cataract operations done between 1 January to 31 December 2019.

The subsidiary objectives.

1. To describe the association between age, gender and the reasons for poor or borderline surgical outcomes at Nkhoma Hospital.
2. To assess the association between the type of surgeon conducting surgery and the reasons for poor or borderline quality of cataract surgery.
3. To assess the association between route / mechanism of referral of patients for cataract surgery and the reasons for poor or borderline quality of cataract surgery.at Nkhoma Hospital
4. To explore the most common cataract surgical complications at Nkhoma Hospital.

The findings of this study provide valuable data for devising effective strategies aimed at addressing the underlying causes of poor or borderline cataract surgical outcomes. Through the application of these strategies, the quality of cataract surgery can significantly be enhanced, resulting in reduction of avoidable blindness due to cataract in Malawi.

Materials and Methods

Nkhoma Hospital situated 80km south of Lilongwe, the capital of Malawi, has been providing high volume cataract surgical service for over twenty years. People requiring cataract surgery are identified and referred to Nkhoma Hospital from all three regions of the country via four

mechanisms, namely by cataract case finders, by an NGO screening project, through Nkhoma Hospital outreach clinic and by self-referral. Three cataract surgeons, comprised of an ophthalmologist and two cataract surgeons, are responsible for a cataract surgical output of approximately 4000 per year.

This study used a quantitative, descriptive design, using data of patients who had undergone cataract surgery at Nkhoma Hospital in Malawi, from January to December 2019. Records of all people who had undergone cataract surgery from 1 January to 31 December and had poor or borderline outcomes in at least one eye were included in the sample, a total of 828 people had poor or borderline outcomes after surgery. And, all the records of cataract people that had surgery at Nkhoma Hospital from 1 January to 31 December 2019 and had a visual acuity outcome of 6/18 and better were excluded from the study.

Information was extracted from hospital record books into the data capture form and were captured into a Microsoft Excel (Microsoft Corporation, 2018. *Microsoft Excel*, Available at: https://office.microsoft.com/excel) spreadsheet using double-entry method by the researcher and an assistant. Data collected included demographics (age, gender), date of operation, referral route and information about preoperative, intraoperative, and post-operative findings. Pre-operative examination information included pre-operative VA, pre-operative intra ocular pressure, biometry and ocular comorbidity. Intra-operative information included date of surgery, surgical technique, intraocular lens position, method of capsulotomy, use of sutures, intraoperative complications. Post-operative examination included: post-operative VA and complications after surgery. People' ages were grouped into 10-year age groups and under 50 years and above 50 years of age.

A variable called Reasons was created to contain the reasons for poor outcomes, derived from information regarding pre- and post-op visual acuities, biometry done, presence of intra-

operative complications, ocular co-morbidity and other determinants of poor vision, according to the key in Table 1.

Table 1: Reasons for poor or borderline outcomes after cataract surgery

Reasons	**Primary Determinant**
Spectacles	Post-operative BCVA corrected to 6/18 or better
Surgery	Intra-operative complications or post-op VA / BCVA worse than pre-op
Selection	Ocular comorbidity known to cause vision loss and other comorbidity likely to affect vision adversely
Screening	Pre-op VA corrected to 6/18 or better

A commonly encountered reason for long-term post-operative complications also known as "sequalae", could not be determined, as the study used records of patients at 24 hours after surgery. The reasons were determined by a senior government ophthalmologist and verified by the lead ophthalmologist based at Nkhoma Hospital.

The data was formatted and cleaned for analysis with STATA 17 (Stata Corp. 2021.Stata Statistical Software: Release 17. College Station, TX: Stata Corp LLC). Descriptive statistical analysis was performed and presented in tables and graphs, inferential statistics such Mas chi-square analysis was conducted to compare the surgery outcome of the age groups and the two genders.

The data collection and analysis posed no risk or discomfort to people as the primary source of data was theatre records. To ensure protecting patient's identities, data was anonymized before data analysis. Prior to the study, approval was sought from University of Cape Town Human Research Ethics Committee, National Health Research Ethics of Malawi, with no informed consent required.

Results

Sample characteristics

Records of all people who had undergone cataract surgery from 1 January to 31 December and had poor or borderline outcomes in at least one eye were included in the sample, a total of 828 people.

Table 2: presents the breakdown of participants categorized by gender and age.

Gender	**Age**		
	<50	**≥50**	**Total**
Female	17	375	392
%	4.3	95.7	100.0
Male	23	413	436
%	5.3	94.7	100.0
Total	40	788	828
%	4.8	95.2	100.0

There were more females aged over 50 (95.7%) than males of the same age group (94.7%).

Table 3 displays the patient distribution according to age groups and referral institutions. The highest proportion of people (40.7%) were referred by MACOHA (Malawi Council for the Handicapped), the cataract case-finding and outreach clinics contributed 23.0% and 26.2% respectively and self-referral contributed 10.1%.

Table 3: Distribution of people by age-group and referral route.

AGE	**REFERRAL**				
	Cataract Case Finder	**MACOHA**	**Outreach clinic**	**Self-referral**	**Total**
<50	5	17	12	6	40
%	12.5	42.5	30.0	15.0	100.00
≥50	185	320	205	78	788
%	23.4	40.6	26.0	9.9	100.00
Total	190	337	217	84	828

%	22.9	40.7	26.2	10.1	100.00

Table 4 illustrates the distribution of vision status in both eyes, categorized by gender. About two-thirds (64.1%) of cataract surgery patients had a pre-operative visual acuity of 6/60 or worse, in other words, blind or severely visually impaired, while 17.1% of patients for cataract surgery had a pre-operative visual acuity of 6/18 or better, in other words, not blind or with early visual impairment. These cases would normally not be eligible for cataract surgery in a setting like Nkhoma Hospital.

Table 4: Distribution of vision Both Eyes (BE) by gender

Vision BE	**Gender**		
	Female	**Male**	**Total**
Blind	148	122	270
%	37.8	28.0	32.6
SVI	117	144	261
%	29.9	33.0	31.5
MVI	69	87	156
%	17.6	20.0	18.9
EVI	24	28	52
%	6.1	6.4	6.3
Not Blind	34	55	89
%	8.7	12.6	10.8
Total	392	436	828
%	100.0	100.0	100.0

Results against each study objectives

Reasons for poor and borderline outcomes

Table 5 illustrates the reasons for poor or borderline outcomes, categorized by region. Selection (ocular comorbidity known to cause vision loss and other comorbidity likely to affect

vision adversely), was the reason for over half (52.2%) of the causes of poor and borderline outcomes after cataract surgery, with Spectacles accounting for a quarter (25.8%) of the poor or borderline outcome.

Table 5: Reasons for poor or borderline cataract surgery outcome versus region

Reason	**Gender**			
	Central	**North**	**South**	**Total**
Selection	384	2	46	432
%	51.0	50.0	64.8	52.2
Screening	35	0	4	39
%	4.7	0.0	5.6	4.7
Spectacles	207	1	6	214
%	27.4	25.0	8.4	25.8
Surgery	29	0	2	31
%	3.8	0.0	2.8	3.7
Unknown	98	1	13	112
%	13.0	25.0	18.3	13.5
Total	753	4	71	828
	100.0	100.0	100.0	100.0

Association with age

Figure 2 illustrates the distribution of reasons for poor or borderline outcomes, categorized by age group. In the 50 years- and- older age groups, the number of patients increased with increase in the age of patients and started to decline with age above 80 years. This is in keeping with the age distribution of cataract surgery patients in general, regardless of outcome.

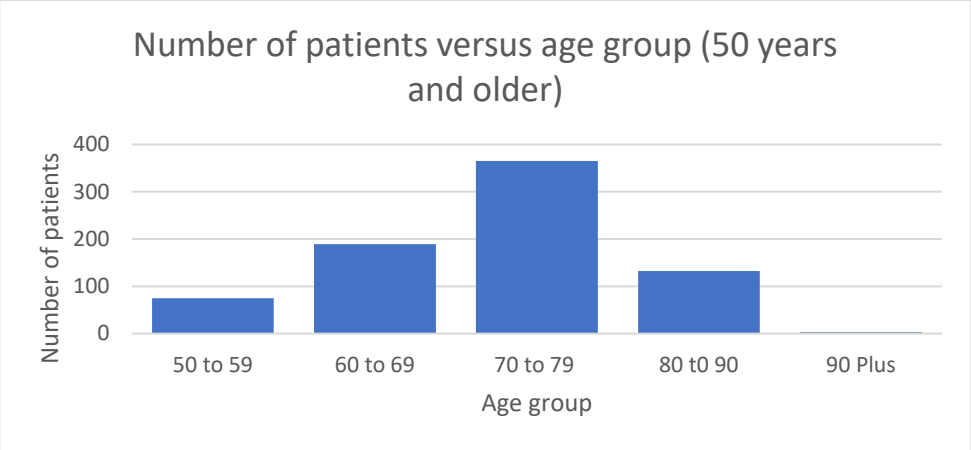

Figure 1: Distribution of reasons according to age group

Association by gender

Table 6 illustrates the distribution of reasons for poor or borderline outcomes, categorized by gender**.** The reasons for poor or borderline cataract surgery outcomes were not significantly differently represented between females and males.

Table 6: Association between gender and reasons for poor or borderline surgery outcomes

Reason	**Gender**		
	Female	**Male**	**Total**
Selection	206	226	432
%	52.6	51.8	52.2
Screening	17	22	39
%	4.3	5.1	4.7
Spectacles	88	126	214
%	22.4	28.9	25.8
Surgery	17	14	31
%	4.3	3.2	3.7
Unknown	64	48	112
%	16.3	11.0	13.5
Total	392	436	828
%	100.0	100.0	100.0

Pearson Chi2 =8.6 Prob=0.073

Association of the type of surgeon conducting surgery

Table 7 illustrates the distribution of reasons for poor or borderline outcomes, categorized by type of surgeon. The cataract surgeons contributed almost 95% of the poor and borderline outcome after cataract surgery. There is insufficient data to determine whether there is a significant association between the outcomes of the cataract surgeons and the ophthalmologist. A Chi-Square p-value of 0.46 shows lack of association between type of surgeon and reasons for poor or borderline outcome of cataract surgery at the hospital.

Table 7: Association between type of the surgeon and the reasons for poor or borderline outcomes

	Surgeon		
Reasons	**Cataract surgeon**	**Ophthalmologist**	**Total**
Selection	409	23	432
%	52.2	52.3	52.2
Screening	39	0	39
%	5.0	0.00	4.7
Spectacles	203	11	214
%	25.9	25.0	25.9
Surgery	28	3	31
%	3.6	6.8	3.7
Unknown	105	7	112
%	13.4	15.9	13.5
Total	784	44	828
%	100.0	100.0	100.0

Pearson Chi2 =3.6 Prob=0.467

Association of the type of referral route

Table 8 illustrates the distribution of reasons for poor or borderline outcomes, categorized by route of referral. Selection (52.2 %) and Spectacles (25.8 %) were the most common reasons for poor and borderline outcomes, with the referral routes “Cataract case finder” and “Outreach clinic” contributing 56.3% and 59.4% of their respective totals to “Selection”. The “MACOHA and “Self”

referral routes contributed the highest proportion of poor and borderline outcomes because of "Spectacles". However, there is no significant association between type of referral route and reasons for poor or borderline outcomes.

Table 8: Reasons for poor or borderline according to referral route

Reasons	**Referral Route**				
	Cataract Case Finder	**MACOHA**	**Outreach clinic**	**Self**	**Total**
Selection	107	156	129	40	432
%	24.7	36.1	29.8	9.2	100.00
Screening	5	15	16	3	39
%	12.8	38.4	41.0	7.6	100.00
Spectacles	51	104	33	26	214
%	23.8	48.6	15.4	12.1	100.00
Surgery	6	12	10	3	31
%	19.3	38.7	32.2	9.6	100.00
Unknown	21	50	29	12	112
%	18.7	44.6	25.8	10.7	100.00
Total	190	337	217	84	828
	22.9	40.7	26.2	10.1	100.00

Pearson Chi2=26.4 prob=0.010

The data revealed a spectrum of complications associated with cataract surgery, which can be categorised according to the affected site/ structure. Thus, complications affecting the whole globe, Cornea, Lens, Uvea and Retina.

Figure 9 illustrates the distribution of complications of surgery related to the ocular structures. The majority (76.38%) of surgical complications in patients with poor or borderline surgical outcomes affected the cornea. 15.95% affected the whole globe structures, 6.75% affected the lens 0.61% affected the uvea and 0.31% affected the retina.

Table 9: Anatomical presentation of complications of cataract surgery causing poor or borderline surgical outcomes.

Site	Complications(n)	Percentage (%)
Whole globe	52	15.95
Cornea	249	76.38
Lens	22	6.75
Uvea	2	0.61
Retina	1	0.31
Total	326	100

Limitations and Assumptions

The findings should be read in consideration of the limitations of the study, namely incomplete and inconsistent record-keeping, derivative methods used to classify reasons for poor or borderline outcomes after cataract surgery, that the visual acuity readings were taken at 24 hours after cataract surgery, and that no long-term consequences of cataract surgery could be recorded.

Data collected at outpatients, theatre and the wards following cataract surgery may not have been complete, resulting in missing data, which in turn affected the way the reasons for poor or borderline cataract surgery outcomes was arrived at. Inconsistent recording of data, especially related to complications, may have affected the computation of frequencies to determine the most common complications. Poor record keeping errors that were evident during data correction is also one of the limiting factors in this study as some records did not have the required information which could introduce various biases such as recall, reasoning and reviewer from the researcher in making decisions to code the reasons resulting in the disproportionately distribution amongst the other causes, effectively changing the ultimate findings.

The algorithms used to determine the reasons for poor or borderlines cataract surgery outcomes followed interpretation commonly used in ophthalmic surgery quality management. When insufficient data is available, however, accurate determinations cannot be made. With more complete information, any of the 13.5% "unknown" reasons could be classified as either "selection",

"spectacles", "surgery" or "screening", thus changing the representation of reasons for poor and borderline outcomes after cataract surgery. This is a limiting factor because the unknown percentage can affect the distribution of other causes if more details were available.

The WHO recommendation for cataract surgery outcomes is standardised at eight weeks after surgery. The visual acuity readings for this study were considered at one day after cataract surgery. A significant proportion of patients can be expected to return improved post operative visualisation acuities six to eight weeks postoperatively.

As this study used one-day visual acuity results, no long-term consequences of cataract surgery could be identified. Posterior capsular opacification, a common form of surgical sequelae, usually takes a few weeks to develop, and can be identified at postoperative follow-ups.

We made an assumption that the records as presented for the study was accurate and that no information had been withheld. Data cleaning procedures included filling in missing values, which was confirmed by the lead ophthalmic surgeon

Discussion

We determined the reasons for poor or borderline surgical outcomes in at least one eye of all people who had undergone cataract surgery from 1 January to 31 December 2019, at Nkhoma Hospital in Malawi, a total of 828 people.

Comorbidity (52.2%) was the major reason for poor or borderline outcomes of cataract surgery, followed by uncorrected refractive error (25.8%). For a total of 13.5% of patients, the reason for poor or borderline outcomes could not be determined, as none of the defining information was available. "Surgery" and "screening" made up the rest of the reasons (4.7% and 3.7%) for poor or borderline outcomes after cataract surgery.

Although a small percentage, screening errors can be very costly for the patient (unnecessary cost to be incurred, especially if vision is not restored) and for the programme, which can be avoided through training of both the fieldwork screens and the staff responsible for pre-operative workup at the hospital.

The patients who have definitively been classified as surgery errors may increase if more information about the "unknown" reasons were available. While less prominent than selection and spectacles, surgery errors caused significant cost and risk to the eye care programme and can be minimised through surgical refresher training. (There are now highly effective simulation training programmes available to improve surgeon skills in short time periods).

Doing operations on patients with comorbidity points to a problem in decision-making, which highly experienced surgeons usually avoid, in other words, they do not select them for surgery. Alerting surgeons to the implications of poor selection is the first step towards reducing poor and borderline outcomes. However, setting clear and firm selection criteria may be a more effective step towards improved survival outcomes. Successful high volume cataract surgical services overcome this by defining eligibility as: hyper-mature cataract with visual acuity of<6/60 in the better eye, and with no underlying conditions.

In this study, a total of 17.1% of patients had a pre-operative visual acuity of 6/18 or better. For most non-tertiary-level surgical facilities, this would make these patients ineligible for cataract surgery. It is not surprising therefore, that 42.2 % of these had worse postoperative visual acuities than before the operation. This also represented 9.4% of the total number of worse outcomes in the cohort.

Also, 38.6% of patients operated were not blind or severely visually impaired according to the WHO classification. This is a factor of uncertainty around selection eligibility. Worsening the

vision of people due to non-application of firm eligibility criteria should not be acceptable by any norms. It may also serve as a strong deterrent for uptake of cataract surgical services.

There was no significant association between gender and the reasons for poor or borderline surgical outcomes at Nkhoma Hospital although the cohort contained slightly more females than males. However, it has been shown in RAAB surveys conducted in southern Africa[7]. that cataract surgical coverage is lower in women than in men, and that women encounter more barriers to access cataract surgical services than men. In 2020 in Mozambique, Roba et al showed that 34.9 percent of women were not aware that cataract is treatable compared to 26.3 percent of men. It is for this reason that Khoza et al in their study concluded that knowledge about cataract services should be decentralised to health facilities in the communities through the integration of traditional health systems and conventional health system to overcome myths associated with cataract blindness.

As was expected, almost 95% of the people were 50 years of age and older. This may be a reflection in the total number of surgeries as well, as the occurrence of blindness due to cataract increases sharply in people aged 50 years or older[11]. Similarly, the median age group of people who had cataract surgery is the 60-70 age group, also reflective of the overall pattern.

The two cataract surgeons are responsible for 95% of the poor or borderline outcomes after cataract surgery. Not knowing the actual work allocation for the year (including those with good and very good outcomes), it is not possible to make accurate inferences about the association between the types of surgeons, and the reasons for poor or borderline cataract surgery outcomes.

About two out of five (40.7%) cataract patients with poor or borderline outcomes after cataract surgery at Nkhoma Hospital had been referred by MACOHA, the Malawian Council for the Handicapped. However, no significant association was found between referral route and reason for poor or borderline outcomes.

The most common cataract surgical complications that occurred in patients with poor or borderline outcomes in cataract surgery, presented in the outer layer (59.2%), with hazy cornea the most common (17.2%) Second was corneal scar (15%) a condition manifesting in the eye later. Vitreous loss, a common complication that requires abscessed surgical techniques and equipment, contributed 6% of the complications.

The monitoring of outcomes after cataract surgery is important for determining reasons for poor or borderline surgical outcomes, which can inform managers, donors, and other stakeholders about strategies to improve the quality cataract services.

Furthermore, knowledge of cataract outcomes and the reasons for poor quality can be used to monitor the performance of surgeons, by allowing them about the gaps in their own and team members' skills, as well as errors they may be inclined to make in decision-making regarding if and what type of surgery should be performed, and by whom.

For the entire cataract surgery team, the outcomes monitoring can help to identify or improve screening and referral practices and emphasize the importance of follow-up to identify long-term post operative consequences of cataract surgery, and institute procedures to address them. The need to correct postoperative refractive error may also be suitably justified, so that spectacles can be provided for those with poor or borderline outcomes who tested 6/18 or better. These measures can substantially enhance the efficiency and effectiveness of cataract services.

The results are in agreement with a study done[6] whereby the reasons for poor or borderline outcomes were reported as ocular co-morbidity (Selection, 52.2 %), surgical complications (Surgery, 3.7 %), and uncorrected refractive error (Spectacles,25.8 %). Similar distribution of reasons was also found in the RAAB study done[7] in the southern region of Malawi.

In addition to equipping cataract surgeons with adequate instruments and consumables, there is continued need for high-quality training of surgeons to reduce complications. The quality of

cataract surgery can also be improved through routine monitoring to inform and improve eye care services on programme levels.

Conclusion

Despite the stated limitations and assumptions, the findings clearly show that more than one third (35.9%) of patients operated were not severely visually impaired or blind to cataract, selection and spectacles are the most common reasons for poor or borderline outcomes after cataract surgery, and that outer layer conditions are the most common forms of complications. It was also shown that the reasons for poor or borderline outcomes after cataract surgery were relatively equally distributed according to gender, age group above 50 years and referral route.

The study highlighted the importance of inaccurate, inadequate and inconsistent recording of information to support effective monitoring of cataract surgical outcomes. With proper monitoring, the reasons for poor or borderline cataract surgery outcomes can be accurately determined, and strategies, such as training of cataract case finders (to improve referral), nursing staff (to improve pre-operative preparation), registration clerks (to improve data capture) and ophthalmic surgeons (to improve selection and surgical skills) can be implemented. Furthermore, implementation of suitable referral mechanisms, eligibility criteria and follow-up procedures may further improve cataract surgical outcomes.

The findings are useful to emphasise the importance of monitoring the outcomes of cataract surgery, for the Nkhoma Hospital eye department, the hospital leadership and other stakeholders in Malawi and elsewhere in the region. Hopefully this will encourage stakeholders to incorporate strategies to overcome the reasons for poor and borderline quality of cataract surgery. This will ensure that quality outcomes of cataract surgery improve, hence helping in the elimination of blindness and visual impairment due to cataract in Malawi and the whole region.

Acknowledgements

First and foremost, praises and thanks to God, THE ALMIGHTY, for making it possible for me to study at University of Cape Town, South Africa.

I would like to express my deep and sincere gratitude to my research supervisors, Dr D Minnies, the Director of the Community Eye Health Institute (UCT-CEHI) in the Division of Ophthalmology at the University of Cape Town, South Africa and Professor Khumbo Kalua the Director for Blantyre Institute of Community Ophthalmology, Blantyre, Malawi, *f*or giving me the opportunity to do research and providing invaluable guidance throughout this research. I am extremely grateful for what they have offered me.

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PART C: APPENDICES

Appendix A: Acknowledgement

First and foremost, praises and thanks to God, THE ALMIGHTY, for making it possible for me to study at University of Cape Town, South Africa.

I would like to express my deep and sincere gratitude to my research supervisors, Dr D Minnies, the Director of the Community Eye Health Institute (UCT-CEHI) in the Division of Ophthalmology at the University of Cape Town, South Africa and Professor Khumbo Kalua the Director for Blantyre Institute of Community Ophthalmology, Blantyre, Malawi, *f*or giving me the opportunity to do research and providing invaluable guidance throughout this research. I am extremely grateful for what they have offered me.

Appendix B: Data Capture Forms

Form 1: Data capture form

Variable Name	Value	Options
A. Patient Demographic characteristics		
Name Patient ID		
Age of patient		In years (0-120)
Gender		1 = Male 2 = Female
Marital status		1=Single; 2=Married; 3=Widowed; 4=Divorced 5 Other
District		
TA		
GVH/township		
B. Pre-Operative Conditions		
Where was the patient referred from		1=not referred; 2= Public health centres; 3=private clinic; 4=district hospital 5= central hospital 9= others (specify)
Date of operation		
Pre-operative Visual acuity RE		6/6, 6/9, 6/12, 6/18, 6/18, 6/24, 6/36 and 6/60
Pre-operative Visual acuity LE		6/6, 6/9, 6/12, 6/18, 6/18, 6/24, 6/36 and 6/60
Pre-operative Intraocular pressure RE		10-21 mm Hg
Pre-operative Intraocular pressure LE		10- 21mmHg
Eye operated		Right or left

Type of operation		Extracapsular cataract extraction (ECCE) and phacoemulsification
Surgeon		Ophthalmologist or cataract surgeon
Type of capsulotomy		suture less or not
IOL inserted?		Yes or No
Type of sutures used		
Second eye?		
Biometry done?		Yes or No
IOL dioptre		17 - 22 mm
Intra-operative complication?		
Other?		specify
Post-operative VA (24 hours) presenting		
Post-operative VA (24 hours) best-corrected		
Post-operative VA (other) presenting		
Co-morbidity?		
Post-operative complications		
Spectacles needed?		Yes or No
Spectacles supplied?		Yes or No

Form 2: Key Informant Interview Guide

Nkhoma eye hospital cataract surgeons Key Informant Interview
Introduction
Thank you for your time. My name is **Martha Chingwengwe** I am currently a student at University of Cape Town doing research as a partial fulfilment for a qualification Master of Public Health in Community Eye Health. The research aims at finding reasons for poor or borderline surgical outcomes at your facility. The goal of this discussion is to learn from you on various issues that can result in the poor or borderline surgical outcomes in patients that had cataract surgery at your facility. Your truthful responses will help the researcher, your facility as well as the whole country on ways to improve cataract services. Please note that your responses will be treated as confidential. Are you willing to take part in the discussions? Again, thank you for your time.
<u>Part A: BACKGROUND INFORMATION</u> (*each field must be filled before interview*)
Date of cataract surgeon
Surgeon's name
Surgeons' education
Age of a patient having surgery
Mode of referral of the patient
Was the surgery perfumed in both eyes
Sex of the cataract surgeon
Part B: Coherence and Institutional Arrangement
1. Do you think this facility is achieving good outcomes of surgery? 2. What do you think are key reasons to achieve good outcomes at this facility? 3. Do you think Nkhoma hospital has poor or borderline surgical outcomes? 4. What are/were key reasons for poor or borderline outcomes? 5. How do you think the poor or borderline surgical outcomes can be resolved/achieved?

6. Do you require external funding to improve on surgical outcomes?
7. Which specific stakeholders do you think would be valuable to reduce poor or borderline cataract surgical outcomes at Nkhoma?
8. In your informed opinion, who are patients at risk of having poor or borderline outcome after cataract surgery?
9. Can you describe how patients are selected for surgery?
10. Can you describe on the availability of surgical equipment used during surgery?

Thank you for your time, we might contact you again to seek further information or clarification later

Appendix C: Ethical Approval Letters

Letter 1: Approval from University of Cape Town

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UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building

Groote Schuur Hospital

Observatory 7925

Telephone [021] 406 6492

Email: hrec-submissions@uct.ac.za

Website: https://health.uct.ac.za/home/human-research-ethics

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28 October 2022

HREC REF: 667/2022

Dr D Minnies

Department of Surgery

J-Floor OMB

Email: d.minnies@uct.ac.za

Student: machingwengwe@gmail.com

Dear Dr Minnies

PROJECT TITLE: REASONS FOR POOR OR BORDERLINE CATARACT SURGICAL OUTCOMES AT NKHOMA HOSPITAL, MALAWI: A RETROSPECTIVE ANALYSIS

(MASTERS CANDIDATE-MRS MARTHA CHINGWENGWE)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study, subject to all local approvals

Approval is granted for one year until the 30 October 2023.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics forms)

The HREC acknowledge that the student: Mrs Martha Chingwenge will also be involved in this study.

Please quote the HREC REF 667/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely Signed by candidate

PROFESSOR M BLOCKMAN

CHAIRPERSON. FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DOH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH

Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Letter 2: Approval from Nkhoma Hospital Research Ethics Committee, Malawi

Nkhoma CCAP Hospital

Ref.27/04/2023 **27th April, 2023.**

To : **Martha Chingwengwe**

Dear Madam,

RE: RE: INSTITUTIONAL PERMISSION TO CONDUCT A STUDY

On behalf of Nkhoma Mission Hospital, I would like to grant you permission for a study entitled **"Determining reasons for poor or borderline cataract surgical outcome"** at Nkhoma Mission Hospital.

Furthermore, I would like to request you to share the findings of this study with Nkhoma Mission Hospital for records and implementation.

Wishing you all the best in your studies.

Yours faithfully,

Signed by candidate

PRINCIPAL NURSING OFFICER NKHOMA C.C.A.P HOSPITAL 27 APR 2023 P.O. BOX 48, NKHOMA

Paul Mekani (MPH, BSc-N, Dip-N&M, Cert.-N&M),

Principal Nursing & Midwifery Officer & Chairperson for Research Committee

Nkhoma Mission Hospital,

P.O. Box 48, Nkhoma, Lilongwe.

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"serving with Love and Care"

Letter 3: Approval from the National Health Sciences Research Committee, Malawi.

Telephone: + 265 1 789 400
Facsimile: + 265 1 789 431
E-mail: research@mail.gov.mw

All Communications should be addressed to: The Secretary for Health

In reply please quote No. MED/4/36c
Ministry of Health
P.O. Box 30377
Lilongwe 3
Malawi

Ref. No. MED/4/36c

2nd June, 2023

Martha Chingwengwe
Malawi College of Health Sciences

Dear Sir/Madam

RE: Protocol # 23/04/4057: Reasons for Poor or Borderline Cataract Surgical Outcomes at Nkhoma Hospital in Malawi: A Retrospective Analysis

Thank you for the above titled proposal that researcher submitted to the National Health Sciences Research Committee (NHSRC) for review. Please be advised that the NHSRC has **reviewed** and **approved** the above-named study.

- **APPROVAL NUMBER** **:4057**
- The above details should be used on all correspondences, consent forms and documents as appropriate.
- **APPROVAL DATE** **:02/06/2023**
- **EXPIRATION DATE** **:01/06/2024**
  This approval expires on **02/06/2024**. After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the NHSRC Secretariat should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING:** All serious problems having to do with subject safety must be reported to the NHSRC within 2 working days using standard forms obtainable from the NHSRC Secretariat.
- **MODIFICATIONS**: Prior NHSRC approval using forms obtainable from the NHSRC Secretariat is required before implementing any changes in the protocol (including changes in the consent documents). You may not use any other consent documents besides those approved by the NHSRC.
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the NHSRC using standard forms obtainable from the NHSRC Secretariat.
- **QUESTIONS**: Please contact the NHSRC on phone number *+265 999397913* or by email on mohdoccentre@gmail.com.
- **OTHER**: Please be reminded to send in copies of your final research results for our records (Health Research Database)

Kind regards from the NHSRC Secretariat.

Signed by candidate

.....

CHAIRPERSON, NATIONAL HEALTH SCIENCES RESEARCH COMMITTEE
Promoting Ethical Conduct of Research [1]

National Health Sciences Research Committee
2023 -06- 02
APPROVED

1

Appendix D: Instructions For Authors PLOS One

***PLOS ONE* Manuscript Guidelines**

(copied from the PLOS ONE website)

o Blots and Gels

o Antibodies

o Systematic Review/Meta-Analysis

o Palaeontology and Archaeology Research

o Software Papers

o Database Papers

o New Zoological Taxon

o New Botanical Taxon

o New Fungal Taxon

o Qualitative Research

1. Format Requirements

PLOS ONE does **not** consider presubmission inquiries. All submissions should be prepared with the following files:

 Cover letter

 Manuscript, including tables and figure legends

 Figures (guidelines for preparing figures can be found at the Figure and Table Guidelines)

Prior to submission, authors who believe their manuscripts would benefit from professional editing is encouraged to use language-editing and copyediting services. Obtaining this service is the responsibility of the author, and should be done before initial submission. These services can be found on the web using search terms like "scientific editing service" or "Manuscript editing service." Submissions are **not** copyedited before publication.

In addition to the guidelines below, please refer to our downloadable sample files to make sure that your submission meets our formatting requirements:

 Download sample title, author list, and affiliations page (PDF)

 Download full manuscript sample (PDF)

Submissions that do not meet the *PLOS ONE* Publication Criterion for language standards

may be rejected.

Cover Letter

You should supply an approximately one-page cover letter that:

- Concisely summarizes why your paper is a valuable addition to the scientific literature
- Briefly relates your study to previously published work
- Specifies the type of article you are submitting (for example, research article, systematic review, meta-analysis, clinical trial)
- Describes any prior interactions with PLOS regarding the submitted manuscript
- Suggests appropriate *PLOS ONE* Academic Editors to handle your manuscript (view a complete listing of our academic editors)
- Lists any opposed reviewers

Your cover letter should **not** include requests to reduce or waive publication fees. Should your manuscript be accepted, you will have the opportunity to include your requests at that time. See *PLOS ONE* Editorial Policy for more information regarding publication fees.

Manuscript Organization

PLOS ONE considers manuscripts of any length. There are no explicit restrictions for the number of words, figures, or the length of the supporting information, although we encourage a concise and accessible writing style. We will **not** consider monographs.

All manuscripts should be double-spaced and include line numbers and page numbers.

Manuscripts should begin with the ordered sections:

- Title
- Authors
- Affiliations
- Abstract
- Introduction

and end with the sections of:

- Acknowledgments
- References
- Supporting Information Captions

Figures should be cited in ascending numeric order upon first appearance. Each figure caption should then be inserted immediately after the first paragraph in which it is cited in the article file.

Figures should not be included in the main manuscript file. Each figure must be prepared and submitted as an individual file. Find more information about preparing figures here.

Tables should be cited in ascending numeric order upon first appearance. Each table should then be inserted immediately after the first paragraph in which it is cited in the article file.

The title, authors, and affiliations should all be included on a title page as the first page of the manuscript file.

There are no explicit requirements for section organization between these beginning and ending sections. Articles may be organized in different ways and with different section titles, according to the authors' preference. In most cases, internal sections include:

- Materials and Methods
- Results
- Discussion
- Conclusions (optional)

PLOS ONE has no specific requirements for the order of these sections, and in some cases it may be appropriate to combine sections. Guidelines for individual sections can be found below.

Abbreviations should be kept to a minimum and defined upon first use in the text. Nonstandard abbreviations should not be used unless they appear at least three times in the text.

Standardized nomenclature should be used as appropriate, including appropriate usage of species names and SI units.

PLOS articles do not support text footnotes. If your accepted submission contains footnotes,

you will be asked to move that material into either the main text or the reference list, depending on the content.

Manuscript File Requirements

Authors may submit their manuscript files in Word (as .doc or .docx), LaTeX (as .pdf), or RTF format. Word files must not be protected.

LaTeX Submissions. If you would like to submit your manuscript using LaTeX, you must author your article using the *PLOS ONE* LaTeX template and Bib Tex style sheet. Articles prepared in LaTeX may be submitted in PDF format for use during the review process. After acceptance, however, .tex files will be required. Please consult our LaTeX guidelines for a list of what will be required.

Microsoft Word Submissions with Equations. If your manuscript is or will be in Microsoft Word and contains equations, you must follow the instructions below to make sure that your equations are editable when the file enters production.

1. Format display equations only in Math Type (http://www.dessci.com/en/products/mathtype/).
2. Inline equations should be completely input via Math Type. Do not include an equation that is part text, part Math Type.
3. Do not use graphic objects.

If you have already composed your article in Microsoft Word and used its built-in equation editing tool, your equations will become unusable during the typesetting process. To resolve this problem, re-key your equations using Math Type.

If you do not follow these instructions, PLOS will not be able to accept your file.

2. Guidelines for Standard Sections

Title

Manuscripts must be submitted with both a full title and a short title, which will appear at the top of the PDF upon publication if accepted. Only the full title should be included in the

manuscript file; the short title will be entered during the online submission process.

The full title must be 250 characters or fewer. It should be specific, descriptive, concise, and comprehensible to readers outside the subject field. Avoid abbreviations if possible. Where appropriate, authors should include the species or model system used (for biological papers) or type of study design (for clinical papers).

Examples:

 Impact of Cigarette Smoke Exposure on Innate Immunity: A *Caenorhabditis elegans* Model

 Solar Drinking Water Disinfection (SODIS) to Reduce Childhood Diarrhoea in Rural Bolivia: A Cluster-Randomized, Controlled Trial

The short title must be 50 characters or fewer and should state the topic of the paper.

Authors and Affiliations

All author names should be listed in the following order:

 First names (or initials, if used),

 Middle names (or initials, if used), and

 Last names (surname, family name)

Each author should list an associated department, university, or organizational affiliation and its location, including city, state/province (if applicable), and country. If the article has been submitted on behalf of a consortium, all author names and affiliations should be listed at the end of the article.

This information cannot be changed after initial submission, so please ensure that it is correct.

To qualify for authorship, one should contribute to **all** of the following:

1. Conception and design of the work, acquisition of data, or analysis and interpretation of data

2. Drafting the article or revising it critically for important intellectual content

3. Final approval of the version to be published

4. Agreement to be accountable for all aspects of the work

All persons designated as authors should qualify for authorship, and all those who qualify should be listed. Each author must have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Those who contributed to the work but do not qualify for authorship should be listed in the acknowledgments.

When a large group or centre has conducted the work, the author list should include the individuals whose contributions meet the criteria defined above, as well as the group name.

All authors must approve the final manuscript before submission. PLOS ONE will contact all authors by email at submission to ensure that they are aware of the submission of the manuscript.

One author should be designated as the corresponding author, and his or her email address or other contact information should be included on the manuscript cover page. This information will be published with the article if accepted.

See the PLOS Editorial and Publishing Policies for more information.

Abstract

The abstract should:

- Describe the main objective(s) of the study
- Explain how the study was done, including any model organisms used, without methodological detail
- Summarize the most important results and their significance
- Not exceed 300 words

Abstracts should **not** include:

- Citations
- Abbreviations, if possible

Introduction

The introduction should:

- Provide background that puts the manuscript into context and allows readers outside the field to understand the purpose and significance of the study
- Define the problem addressed and why it is important
- Include a brief review of the key literature
- Note any relevant controversies or disagreements in the field
- Conclude with a brief statement of the overall aim of the work and a comment about whether that aim was achieved

Materials and Methods

This section should provide enough detail to allow suitably skilled investigators to fully replicate your study. Specific information and/or protocols for new methods should be included in detail. If materials, methods, and protocols are well established, authors may cite articles where those protocols are described in detail, but the submission should include sufficient information to be understood independent of these references.

We encourage authors to submit detailed protocols for newer or less well-established methods as Supporting Information. Further information about formatting Supporting Information files, can be found here.

Methods sections of papers on research using **human or animal subjects and/or tissue or field sampling** must include required ethics statements. See the Reporting Guidelines for human research, clinical trials, animal research, and observational and field studies for more information.

Methods sections of papers with **data that should be deposited in a publicly available database** should specify where the data have been deposited and provide the relevant accession numbers and version numbers, if appropriate. Accession numbers should be provided in parentheses after the entity on first use. If the accession numbers have not yet been obtained at the time of submission, please state that they will be provided during review. They must be provided prior to publication. A list of recommended repositories for different

types of data can be found here.

Methods sections of papers using **cell lines** must state the origin of the cell lines used. See the Reporting Guidelines for cell line research for more information.

Methods sections of papers adding **new taxon names** to the literature must follow the Reporting Guidelines below for a new zoological taxon, botanical taxon, or fungal taxon.

Results, Discussion, and Conclusions

These sections may all be separate, or may be combined to create a mixed Results/Discussion section (commonly labelled "Results and Discussion") or a mixed Discussion/Conclusions section (commonly labelled "Discussion"). These sections may be further divided into subsections, each with a concise subheading, as appropriate. These sections have no word limit, but the language should be clear and concise.

Together, these sections should describe the results of the experiments, the interpretation of these results, and the conclusions that can be drawn. Authors should explain how the results relate to the hypothesis presented as the basis of the study and provide a succinct explanation of the implications of the findings, particularly in relation to previous related studies and potential future directions for research.

PLOS ONE editorial decisions do not rely on perceived significance or impact, so authors should avoid overstating their conclusions. See the *PLOS ONE* Publication Criteria for more information.

Acknowledgments

People who contributed to the work but do not fit the *PLOS ONE* authorship criteria should be listed in the acknowledgments, along with their contributions. You must ensure that anyone named in the acknowledgments agrees to being so named.

Funding sources should **not** be included in the acknowledgments, or anywhere in the manuscript file. You will provide this information during the manuscript submission process.

References

General guidelines

- PLOS uses the reference style as outlined in the ICMJE sample references, also referred to as the "Vancouver" style.
- References must be listed at the end of the manuscript and numbered in the order that they appear in the text.
- In the text, citations should be indicated by the reference number in brackets.
- Authors may cite any and all available works in the reference list.
- Authors may not cite unavailable and unpublished work, including manuscripts that have been submitted but not yet accepted (e.g., "unpublished work," "data not shown").
- If an article is submitted to a journal and also publicly available as a pre-print, the preprint may be cited.
- If related work has been submitted to PLOS ONE or elsewhere, authors should include a copy with the submitted article as confidential supplementary information, for review purposes only.
- Authors should not state 'unpublished work' or 'data not shown,' but instead include those data as supplementary material or deposit the data in a publicly available database.
- Journal name abbreviations should be those found in the NCBI databases.

Reference formatting

Because all references will be linked electronically as much as possible to the papers they cite, proper formatting of the references is crucial. References should be formatted as follows:

Published papers

1. Hou WR, Hou YL, Wu GF, Song Y, Su XL, Sun, B, et al. cDNA, genomic sequence cloning and overexpression of ribosomal protein gene L9 (rpL9) of the giant panda

(*Ailuropoda melanoleuca*). Genet Mol Res. 2011;10: 1576-1588.

Note: Use of a DOI number for the full-text article is acceptable as an alternative to or in addition to traditional volume and page numbers:

Devaraju P, Gulati R, Antony PT, Mithun CB, Negi VS. Susceptibility to SLE in South Indian Tamils may be influenced by genetic selection pressure on TLR2 and TLR9 genes. Mol Immunol. 2014 Nov 22. pii: S0161-5890(14)00313-7. doi: 10.1016/j.molimm.2014.11.005

Accepted, unpublished papers

Same as above, but "In press" appears instead of the page numbers or DOI.

Websites or online articles

1. Huynen MMTE, Martens P, Hilde link HBM. The health impacts of globalisation: a conceptual framework. Global Health. 2005;1: 14. Available: http://www.globalizationandhealth.com/content/1/1/14.

Books

1. Bates B. Bargaining for life: A social history of tuberculosis. 1st ed. Philadelphia: University of Pennsylvania Press; 1992.

Book chapters

1. Hansen B. New York City epidemics and history for the public. In: Harden VA, Risse GB, editors. AIDS and the historian. Bethesda: National Institutes of Health; 1991. pp. 21-28.

Deposited articles (preprints, e-prints, or arXiv)

1. Krick T, Shub DA, Verstraete N, Ferreiro DU, Alonso LG, Shub M, et al. Amino acid metabolism conflicts with protein diversity; 1991. Preprint. Available: arXiv:1403.3301v1. Accessed 17 March 2014.

Published media (print or online newspapers and magazine articles)

1. Fountain H. For Already Vulnerable Penguins, Study Finds Climate Change Is Another Danger. The New York Times. 29 Jan 2014. Available: http://www.nytimes.com/2014/01/30/science/earth/climate-change-taking-toll-on-penguinsstudy-finds.html. Accessed 17 March 2014.

New media (blogs, websites, or other written works)

1. Allen L. Announcing PLOS Blogs. 2010 Sep 1 [cited 17 March 2014]. In: PLOS Blogs [Internet]. San Francisco: PLOS 2006 - . [about 2 screens]. Available: http://blogs.plos.org/plos/2010/09/announcing-plos-blogs/.

Masters' theses or doctoral dissertations

1. Wells A. Exploring the development of the independent, electronic, scholarly journal. M.Sc. Thesis, The University of Sheffield. 1999. Available: http://cumincad.scix.net/cgibin/works/Show?2e09.

Databases and repositories (Fig share, arXiv)

1. Roberts SB. QPX Genome Browser Feature Tracks; 2013. Database: fig share [Internet]. Accessed: http://figshare.com/articles/QPX_Genome_Browser_Feature_Tracks/701214.

Multimedia (videos, movies, or TV shows)

1. Hitchcock A, producer and director. Rear Window [Film]; 1954. Los Angeles: MGM.

Figure Legends

Figures should **not** be included in the manuscript file, but figure legends should be. Guidelines for preparing figures can be found here.

Figure legends should describe the key messages of a figure. Legends should have a short title of 15 words or less. The full legend should have a description of the figure and allow readers to understand the figure without referring to the text. The legend itself should be succinct, avoid lengthy descriptions of methods, and define all non-standard symbols and abbreviations.

Figures should be cited in ascending numeric order upon first appearance. Each figure caption should be inserted immediately after the first paragraph in which they are cited in the article file. Further information about figure captions can be found in the Figure Guidelines.

Supporting Information Captions

Because Supporting Information is accessed via a hyperlink attached to its captions, captions

must be listed in the article file. Do not submit a separate caption file. It is acceptable to have them in the file itself in addition, but they must be in the article file for access to be possible in the published version.

The file category name and number is required, and a one-line title is highly recommended. A legend can also be included but is not required. Supporting Information captions should be formatted as follows.

S1 Text. Title is strongly recommended. Legend is optional.

Please see our Supporting Information guidelines for more details.

Data Reporting Guidelines

All data and related metadata underlying the findings reported in a submitted manuscript should be deposited in an appropriate public repository, unless already provided as part of the submitted article. Repositories may be either subject-specific (where these exist) and accept specific types of structured data, or generalist repositories that accept multiple data types. We recommend that authors select repositories appropriate to their field. Repositories may be subject-specific (eg, GenBank for sequences and PDB for structures), general, or institutional, as long as DOIs or accession numbers are provided and the data are at least as open as CCBY. Authors are encouraged to select repositories that meet accepted criteria as trustworthy digital repositories, such as criteria of the Centre for Research Libraries or Data Seal of Approval. Large, international databases are more likely to persist than small, local ones.

To support data sharing and author compliance of the PLOS data policy, we have integrated our submission process with a select set of data repositories. The list is neither representative nor exhaustive of the suitable repositories available to authors. Current repository integration partners include: Dryad and figshare. Please contact data@plos.org to make recommendations for further partnerships.

Instructions for PLOS submissions with data deposited in an integration partner repository:

Deposit data in the integrated repository of choice. Once deposition is final and complete, the

repository will provide the author with a dataset DOI (provisional) and private URL for reviewers to gain access to the data. Enter the given data DOI into the full Data Availability Statement, which is requested in the Additional Information section of the PLOS Submission form. Then provide the URL passcode in the Attach Files section. If you have any questions, please contact us at plosone@plos.org

Accession Numbers

All appropriate datasets, images, and information should be deposited in public resources. Please provide the relevant accession numbers (and version numbers, if appropriate). Accession numbers should be provided in parentheses after the entity on first use. Suggested databases include, but are not limited to:

- Array Express
- Bio Models Database
- Database of Interacting Proteins
- DNA Data Bank of Japan [DDBJ]
- DRYAD
- EMBL Nucleotide Sequence Database
- GenBank
- Gene Expression Omnibus [GEO]
- Protein Data Bank
- Uni Prot KB/Swiss-Prot
- ClinicalTrials.gov

In addition, as much as possible, please provide accession numbers or identifiers for all entities such as genes, proteins, mutants, diseases, etc., for which there is an entry in a public database, for example:

- Ensemble
- Entrez Gene
- Fly Base

- InterPro
- Mouse Genome Database (MGD)
- Online Mendelian Inheritance in Man (OMIM)
- PubChem

Providing accession numbers allows linking to and from established databases and integrates your article with a broader collection of scientific information.

Striking Images

Authors are encouraged to upload a "striking image" that may be used to represent their paper online in places like the journal homepage or in search results. The striking image must be derived from a figure or supporting information file from the paper, ie. a cropped portion of an image or the entire image. Striking images should ideally be high resolution, eye-catching, single panel images, and should ideally avoid containing added details such as text, scale bars, and arrows. If no striking image is uploaded, a figure from the paper will be designated as the striking image.

Please keep in mind that PLOS's Creative Commons Attribution License applies to striking images. As such, do not submit any figures or photos that have been previously copyrighted unless you have express written permission from the copyright holder to publish under the CCAL license. Note that all published materials in PLOS ONE are freely available online, and any third party is permitted to read, download, copy, distribute, and use these materials in anyway, even commercially, with proper attribution.

Care should be taken with the following image types in particular:

1. PLOS ONE is unable to publish any images generated by Google software (Google Maps, Street View, and Earth)
2. Maps in general are usually copyrighted, especially satellite maps
3. Photographs
4. Commercial or government images, slogans, or logos
5. Images from Facebook or Twitter

Authors must also take special care when submitting manuscripts that contain potentially identifying images of people. Identifying information should not be included in the manuscript unless the information is crucial and the individual has provided written consent by completing the Consent Form for Publication in a PLOS Journal (PDF).

For license inquiries, e-mail license [at] plos.org.

Tables

Tables should be cited in ascending numeric order upon first appearance. Each table should be inserted immediately after the first paragraph in which it is cited in the article file. All tables should have a concise title. Footnotes can be used to explain abbreviations. Citations should be indicated using the same style as outlined above. Tables occupying more than one printed page should be avoided, if possible. Larger tables can be published as Supporting Information. Please ensure that table formatting conforms to our Guidelines for table preparation.

3. Specific Reporting Guidelines

Human Subject Research

Methods sections of papers on research using human subject or samples must include ethics statements that specify:

 The name of the approving institutional review board or equivalent committee(s). If approval was not obtained; the authors must provide a detailed statement explaining why it was not needed

 Whether informed consent was written or oral. If informed consent was oral, it must be stated in the manuscript:

o Why written consent could not be obtained

o That the Institutional Review Board (IRB) approved use of oral consent

o How oral consent was documented

For studies involving humans categorized by race/ethnicity, age, disease/disabilities, religion,

sex/gender, sexual orientation, or other socially constructed groupings, authors should:

- Explicitly describe their methods of categorizing human populations
- Define categories in as much detail as the study protocol allows
- Justify their choices of definitions and categories, including for example whether any rules of human categorization were required by their funding agency
- Explain whether (and if so, how) they controlled for confounding variables such as socioeconomic status, nutrition, environmental exposures, or similar factors in their analysis

In addition, outmoded terms and potentially stigmatizing labels should be changed to more current, acceptable terminology. Examples: "Caucasian" should be changed to "white" or "of [Western] European descent" (as appropriate); "cancer victims" should be changed to "Patients with cancer."

For papers that include identifying, or potentially identifying, information, authors must download the Consent Form for Publication in a PLOS Journal (PDF), which the individual, parent, or guardian must sign once they have read the paper and been informed about the terms of PLOS open-access license. The signed consent form should not be submitted with the manuscript, but authors should securely file it in the individual's case notes and the methods section of the manuscript should explicitly state that consent authorization for publication is on file, using wording like:

The individual in this manuscript has given written informed consent (as outlined in PLOS consent form) to publish these case details.

For more information about *PLOS ONE* policies regarding human subject research, see the Publication Criteria and Editorial Policies.

Clinical Trials

Authors of manuscripts describing the results of clinical trials must adhere to the CONSORT reporting guidelines appropriate to their trial design, available on the CONSORT Statement website. Before the paper can enter peer review, authors must:

1. Provide the registry name and number in the methods section of the manuscript

2. Provide a copy of the trial protocol as approved by the ethics committee and a completed CONSORT checklist as Supporting Information (which will be published alongside the paper, if accepted). This should be named S1 CONSORT Checklist.

3. Include the CONSORT flow diagram as the manuscript's "Fig. 1"

Any deviation from the trial protocol must be explained in the paper. Authors must explicitly discuss informed consent in their paper, and we reserve the right to ask for a copy of the patient consent form.

The methods section must include the name of the registry, the registry number, and the URL of your trial in the registry database for each location in which the trial is registered.

For more information about *PLOS ONE* policies regarding clinical trials, see the Editorial Policies.

Animal Research

Methods sections of manuscripts reporting results of animal research must include required ethics statements that specify:

- The full name of the relevant ethics committee that approved the work, and the associated permit number(s) (where ethical approval is not required, the manuscript should include a clear statement of this and the reason why)
- Relevant details for efforts taken to ameliorate animal suffering

For example:

This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health. The protocol was approved by the Committee on the Ethics of Animal Experiments of the University of Minnesota (Permit Number: 27-2956). All surgery was performed under sodium pentobarbital anaesthesia, and all efforts were made to minimize suffering.

The organism(s) studied should always be stated in the abstract. Where research may be

confused as pertaining to clinical research, the animal model should also be stated in the title.

We ask authors to follow the ARRIVE (Animal Research: Reporting of *In Vivo* Experiments) guidelines for all submissions describing laboratory-based animal research and to upload a completed ARRIVE Guidelines Checklist to be published as supporting information. Please note that inclusion of a completed ARRIVE Checklist will be a formal requirement for publication at a later date.

For more information about *PLOS ONE* policies regarding animal research, see the Publication Criteria and Editorial Policies.

Observational and Field Studies

Methods sections for submissions reporting on any type of field study must include ethics statements that specify:

- Permits and approvals obtained for the work, including the full name of the authority that approved the study; if none were required, authors should explain why
- Whether the land accessed is privately owned or protected
- Whether any protected species were sampled
- Full details of animal husbandry, experimentation, and care/welfare, where relevant

For more information about *PLOS ONE* policies regarding observational and field studies, see the Publication Criteria and Editorial Policies.

Cell Line Research

Authors reporting research using cell lines should state when and where they obtained the cells, giving the date and the name of the researcher, cell line repository, or commercial source (company) who provided the cells, as appropriate. Authors must also include the following information for each cell line:

For *de novo* (new) cell lines, including those given to the researchers a gift, authors must follow our policies for human subject research or animal research, as appropriate. The ethics statement must include:

 Details of institutional review board or ethics committee approval; AND

 For human cells, confirmation of written informed consent from the donor, guardian, or next of kin

For established cell lines, the Methods section should include:

 A reference to the published article that first described the cell line; AND/OR

 The cell line repository or company the cell line was obtained from, the catalogue number, and whether the cell line was obtained directly from the repository/company or from another laboratory

Authors should check established cell lines using the ICLAC Database of Cross contaminated or Misidentified Cell Lines to confirm they are not misidentified or contaminated. Cell line authentication is recommended - e.g. by karyotyping, isozyme analysis, or short tandem repeats (STR) analysis - and may be required during peer review or after publication.

Blots and Gels

Authors of manuscripts reporting results from blots (including Western blots) and electrophoretic gels should follow these guidelines:

 In accordance with *PLOS ONE*'s policy on image manipulation, the image should not be adjusted in any way that could affect the scientific information displayed, e.g. by modifying the background or contrast

 All blots and gels that support results reported in the manuscript should be provided

 Original uncropped and unadjusted blots and gels, including molecular size markers, should be provided in either the figures or the supplementary files

 Lanes should not be overcropped around the bands; the image should show most or all of the blot or gel. Any non-specific bands should be shown and an explanation of their nature should be given

 The image should include all relevant controls, and controls should be run on the same blot or gel as the samples

 A figure panel should not include composite images of bands originating from different blots or gels. If the figure shows non-adjacent bands from the same blot or gel, this should be clearly denoted by vertical black lines and the figure legend should provide details of how the figure was made

Antibodies

Manuscripts reporting experiments using antibodies should include the following information:

 The name of each antibody, a description of whether it is monoclonal or polyclonal, and the host species

 The commercial supplier or source laboratory

 The catalogue or clone number and, if known, the batch number

 The antigen(s) used to raise the antibody

 For established antibodies, authors are encouraged to supply a stable public identifier from the Antibody Registry (www.antibodyregistry.org).

Authors should also report the following experimental details:

 The final antibody concentration or dilution

 A reference to the validation study if the antibody was previously validated, and if not, details of how the authors validated the antibody for the applications and species used. Authors should consider adding information on new validations to a publicly available database such as Antibiotype or CiteAb.

Systematic Review/Meta-Analysis

A systematic review paper, as defined by The Cochrane Collaboration, is a review of a clearly formulated question that uses explicit, systematic methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. These reviews differ substantially from narrative-based reviews or synthesis articles. Statistical methods (meta-analysis) may or may not be used to analyse and

summarize the results of the included studies.

Reports of systematic reviews and meta-analyses must include a completed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist and flow diagram to accompany the main text. Blank templates are available here:

- Checklist: PDF or Word document
- Flow diagram: PDF or Word document

Authors must also state in their "Methods" section whether a protocol exists for their systematic review, and if so, provide a copy of the protocol as Supporting Information and provide the registry number in the abstract.

If your article is a Systematic Review or a Meta-Analysis you should:

- State this in your cover letter
- Select "Research Article" as your article type when submitting
- Include the PRISMA flowchart as Fig. 1 (required where applicable)
- Include the PRISMA checklist as Supporting Information

Meta-Analysis of Genetic Association Studies

Manuscripts reporting a meta-analysis of genetic association studies must report results of value to the field and should be reported according to the guidelines presented in "Systematic Reviews of Genetic Association Studies" by Sagoo *et al.*

On submission, authors will be asked to justify the rationale for the meta-analysis and how it contributes to the base of scientific knowledge in the light of previously published results. Authors will also be asked to complete a checklist outlining information about the justification for the study and the methodology employed. Meta-analyses that replicate published studies will be rejected if the authors do not provide adequate justification.

Palaeontology and Archaeology Research

Manuscripts reporting palaeontology and archaeology research must include descriptions of methods and specimens in sufficient detail to allow the work to be reproduced. Data sets supporting statistical and phylogenetic analyses should be provided, preferably in a format

that allows easy re-use.

Specimen numbers and complete repository information, including museum name and geographic location, are required for publication. Locality information should be provided in the manuscript as legally allowable, or a statement should be included giving details of the availability of such information to qualified researchers.

If permits were required for any aspect of the work, details should be given of all permits that were obtained, including the full name of the issuing authority. This should be accompanied by the following statement:

All necessary permits were obtained for the described study, which complied with all relevant regulations.

If no permits were required, please include the following statement:

No permits were required for the described study, which complied with all relevant regulations.

See the *PLOS ONE* Editorial Policies for more information regarding manuscripts describing palaeontology and archaeology research.

Software Papers

Manuscripts describing software should provide full details of the algorithms designed. Describe any dependencies on commercial products or operating system. Include details of the supplied test data and explain how to install and run the software. A brief description of enhancements made in the major releases of the software may also be given. Authors should provide a direct link to the deposited software from within the paper.

See the *PLOS ONE* Editorial Policies for more information about submitting manuscripts.

Database Papers

For descriptions of databases, provide details about how the data were curated, as well as plans for long-term database maintenance, growth, and stability. Authors should provide a direct link to the database hosting site from within the paper.

See the *PLOS ONE* Editorial Policies for more information about submitting manuscripts describing databases.

New Zoological Taxon

For proper registration of a new zoological taxon, we require two specific statements to be included in your manuscript.

In the **Results** section, the globally unique identifier (GUID), currently in the form of a Life Science Identifier (LSID), should be listed under the new species name, for example:

Anochetus Bolton Fisher **sp. Nov.** urn:lsid:zoobank.org:act:B6C072CF-1CA6-40C7-8396-534E91EF7FBB

You will need to contact Zoo bank to obtain a GUID (LSID). Please do this as early as possible to avoid delay of publication upon acceptance of your manuscript. It is your responsibility to provide us with this information so we can include it in the final published paper.

Please also insert the following text into the **Methods** section, in a sub-section to be called "Nomenclatural Acts":

The electronic edition of this article conforms to the requirements of the amended International Code of Zoological Nomenclature, and hence the new names contained herein are available under that Code from the electronic edition of this article. This published work and the nomenclatural acts it contains have been registered in Zoo Bank, the online registration system for the ICZN. The ZooBank LSIDs (Life Science Identifiers) can be resolved and the associated information viewed through any standard web browser by appending the LSID to the prefix "http://zoobank.org/". The LSID for this publication is: urn: lsid:zoobank.org:pub: XXXXXXX. The electronic edition of this work was published in a journal with an ISSN, and has been archived and is available from the following digital repositories: PubMed Central,

LOCKSS [author to insert any additional repositories].

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New Botanical Taxon

When publishing papers that describe a new botanical taxon, PLOS aims to comply with the requirements of the International Code of Nomenclature for algae, fungi, and plants (ICN). In association with the International Plant Names Index (IPNI), the following guidelines for publication in an online-only journal have been agreed such that any scientific botanical name published by us is considered effectively published under the rules of the Code. Please note that these guidelines differ from those for zoological nomenclature, and apply only to seed plants, ferns, and lycophytes.

Effective January 2012, "the description or diagnosis required for valid publication of the name of a new taxon" can be in either Latin or English. This does not affect the requirements for scientific names, which are still to be Latin.

Also, effective January 2012, the electronic PDF represents a published work according to the ICN for algae, fungi, and plants. Therefore, the new names contained in the electronic publication of a *PLOS ONE* article is effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

Additional information describing recent changes to the Code can be found here.

For proper registration of the new taxon, we require two specific statements to be included in your manuscript.

In the **Results** section, the globally unique identifier (GUID), currently in the form of a Life Science Identifier (LSID), should be listed under the new species name, for example:

Solanum asperum Snapp, sp. nov [urn:lsid:ipni.org:names:77103633-1] Type: Colombia. Putumayo: vertiente oriental de la Cordillera, entre Saccharates y San Francisco de Sibundoy, 1600-1750 m, 30 Dec 1940, J. Cuatrecasas 11471 (holotype,

COL; isotypes, F [F-1335119], US [US-1799731]).

PLOS ONE staff will contact IPNI to obtain the GUID (LSID) after your manuscript is accepted for publication, and this information will then be added to the manuscript during the production phase

In the **Methods** section, include a sub-section called "Nomenclature" using the following wording:

The electronic version of this article in Portable Document Format (PDF) in a work with an ISSN or ISBN will represent a published work according to the International Code of Nomenclature for algae, fungi, and plants, and hence the new names contained in the electronic publication of a *PLOS ONE* article are effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

In addition, new names contained in this work have been submitted to IPNI, from where they will be made available to the Global Names Index. The IPNI LSIDs can be resolved and the associated information viewed through any standard web browser by appending the LSID contained in this publication to the prefix http://ipni.org/. The online version of this work is archived and available from the following digital repositories: [INSERT NAMES OF DIGITAL REPOSITORIES WHERE ACCEPTED MANUSCRIPT WILL BE SUBMITTED (PubMed Central, LOCKSS etc)].

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New Fungal Taxon

When publishing papers that describe a new fungal taxon name, PLOS aims to comply with

the requirements of the International Code of Nomenclature for algae, fungi, and plants (ICN). The following guidelines for publication in an online-only journal have been agreed such that any scientific fungal name published by us is considered effectively published under the rules of the Code. Please note that these guidelines differ from those for zoological nomenclature.

Effective January 2012, "the description or diagnosis required for valid publication of the name of a new taxon" can be in either Latin or English. This does not affect the requirements for scientific names, which are still to be Latin.

Also, effective January 2012, the electronic PDF represents a published work according to the ICN for algae, fungi, and plants. Therefore, the new names contained in the electronic publication of a *PLOS ONE* article is effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

Additional information describing recent changes to the Code can be found here.

For proper registration of the new taxon, we require two specific statements to be included in your manuscript.

In the **Results** section, the globally unique identifier (GUID), currently in the form of a Life Science Identifier (LSID), should be listed under the new species name, for example:

Hymenogaster huthii. Stielow et al. 2010, sp. nov.

[urn:lsid:indexfungorum.org:names:518624]

You will need to contact either Mycobank or Index Fungorum to obtain the GUID (LSID). Please do this as early as possible to avoid delay of publication upon acceptance of your manuscript. It is your responsibility to provide us with this information so we can include it in the final published paper. Effective January 2013, all papers describing new fungal species must reference the identifier issued by a recognized repository in the protologue in order to be considered effectively published.

In the **Methods** section, include a sub-section called "Nomenclature" using the following wording (this example is for taxon names submitted to Myco Bank; please substitute appropriately if you have submitted to Index Fungorum):

The electronic version of this article in Portable Document Format (PDF) in a work with an ISSN or ISBN will represent a published work according to the International Code of Nomenclature for algae, fungi, and plants, and hence the new names contained in the electronic publication of a *PLOS ONE* article are effectively published under that Code from the electronic edition alone, so there is no longer any need to provide printed copies.

In addition, new names contained in this work have been submitted to MycoBank from where they will be made available to the Global Names Index. The unique MycoBank number can be resolved and the associated information viewed through any standard web browser by appending the MycoBank number contained in this publication to the prefix http://www.mycobank.org/MB/. The online version of this work is archived and available from the following digital repositories: [INSERT NAMES OF DIGITAL REPOSITORIES WHERE ACCEPTED MANUSCRIPT WILL BE SUBMITTED (PubMed Central, LOCKSS etc)].

All *PLOS ONE* articles are deposited in PubMed Central and LOCKSS. If your institute, or those of your co-authors, has its own repository, we recommend that you also deposit the published online article there and include the name in your article.

Qualitative Research

Qualitative research studies use non-quantitative methods to address a defined research question that may not be accessible by quantitative methods, such as people's interpretations, experiences, and perspectives. The analysis methods are explicit, systematic, and reproducible, but the results do not involve numerical values or use statistics. Examples of qualitative data sources include, but are not limited to, interviews, text documents, audio/video recordings, and free-form answers to questionnaires and surveys.

Qualitative research studies should be reported in accordance to the Consolidated criteria for

reporting qualitative research (COREQ) checklist. Further reporting guidelines can be found in the Equator Network's Guidelines for reporting qualitative research.