



UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

**POST-OPERATIVE TRACHOMATOUS TRICHIASIS IN AFRICA: A
SYSTEMATIC REVIEW AND ONLINE SURVEY**

By

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SUBMITTED TO THE UNIVERSITY OF CAPE TOWN
In partial fulfilment of the requirements for the degree
Master of Public Health (Community Eye Health track)

Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN

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Date of Submission: 15/01/2019

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DECLARATION

I, *Grace Wangari Mwangi*, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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ACKNOWLEDGEMENTS

First and foremost, I would like to express my deepest and most sincere gratitude to my supervisor, Professor Paul Courtright, for his guidance, encouragement and unwavering support throughout this study. His profound expertise in the study subject and mentorship has illuminated my understanding of the topic and enhanced my research skills.

My sincere appreciation also goes to Dr Anthony Solomon of the World Health Organization for his invaluable contribution in making this research study a reality. His expert guidance, support, and interest in this research have been instrumental in seeing to its successful completion, and for this I am deeply grateful.

I also want to thank the Trachoma National Programme Coordinators in the 29 countries where the survey for this study was conducted for readily and willingly accepting to participate in the survey, to the UCT Library Staff and everyone else who assisted in finding missing articles for the systematic review. Their valuable support towards the completion of this study is greatly appreciated.

To my family – my mother, brother and sisters, I express my utmost thanks for always believing in me. Their unwavering support, reassurance and encouragement have kept me focused and dedicated throughout this journey.

Lastly, my special gratitude goes to the Queen Elizabeth Diamond Jubilee Trust for offering me a scholarship to study at the University of Cape Town, without which none of this would have been possible.

Above all, I give all the glory and adoration to the Almighty God, He who has guided me to every success and accomplishment that I have attained throughout my life, including this one.

SYNOPSIS

This MPH dissertation is a combination of a systematic review of the incidence of postoperative trichiasis and other poor outcomes in Africa, and an online survey of the national approaches to surgical follow up, outcome assessment and audit in trachoma endemic countries within WHO African region.

The main aim of the systematic review was to assess post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa, while the purpose of the online survey was to assess the current national targets for good surgical outcomes, national policies and strategies for monitoring outcomes and conducting surgical audits, and strategies for addressing poor surgical quality among surgeons

Part A of this dissertation is the research protocol, which outlines the background, the methods and materials used to carry out this research.

Part B expounds on the background information based on published literature relating to the subject topic with a full list of references at the end of each section

Part C presents the study findings in a format suitable for submission to the PLOS | One journal. The background of this research project is summarized and the results for both the systematic review and online survey presented and discussed separately.

ABBREVIATIONS

BLTR	Bilamellar Tarsal Rotation
CBAs	Controlled before-and-after studies
CINHAL	Cumulative Index to Nursing and Allied Health Literature
CO	Corneal Opacification
ECAs	Eyelid Contour Abnormalities
GET2020	Global Elimination of Trachoma by 2020
GTMP	Global Trachoma Mapping Project
HEADSTART	Human Eyelid Analogue Device for Surgical Training and skill Reinforcement in Trachoma
ICTC	International Coalition for Trachoma Control
IECWs	Integrated Eye Care Workers
MeSH	Medical Subject Headings
NTDs	Neglected Tropical Disease
PLTR	Posterior Lamellar Tarsal Rotation
PRET	Partnership for the Rapid Elimination of Trachoma
RCT	Randomised Controlled Trials
SAFE	Surgery, Antibiotics, Facial cleanliness, Environmental improvements
STAR	Surgery for Trichiasis, Antibiotics to prevent Recurrence
TT	Trachomatous trichiasis
TTR	Transverse Tarsotomy and lid margin Rotation
UCT	University of Cape Town
WHO	World Health Organization
WHA	World Health Assembly

PART A: STUDY PROTOCOL

TABLE OF CONTENTS

PART I: SYSTEMATIC REVIEW 3

1. BACKGROUND 4

1.1 Introduction..... 4

1.2 Trichiasis Surgery 5

1.3 Surgery outcomes and post-operative trichiasis..... 5

2. PURPOSE..... 6

2.1 Aim 6

2.2 Objectives 6

2.3. Review question..... 6

3. METHODOLOGY 7

3.1 Search Strategy 7

3.2 Inclusion and exclusion criteria 7

3.3 Study selection 8

3.4 Quality assessment..... 8

3.5 Data extraction 8

3.6 Dealing with missing data..... 8

3.7 Data synthesis 8

3.8 Discussion and reporting..... 9

4. ETHICAL APPROVAL 9

PART II. ONLINE SURVEY 10

5. BACKGROUND 11

6. PURPOSE..... 11

2.1 Aim 11

2.2 Objectives 12

7. METHODOLOGY 12

3.1 Study design..... 12

PART A: STUDY PROTOCOL

3.2 Study setting.....	12
3.3 Inclusion and exclusion criteria	12
3.4 Recruitment of participants.....	12
3.5 Data collection	12
3.6 Data entry and analysis	12
8. ETHICAL APPROVAL	12
4.1 Informed consent	13
4.2 Privacy and confidentiality	13
4.3 Potential risk and benefits.....	13
REFERENCES	14
LIST OF APPENDICES.....	17
Appendix 1: Study Eligibility Assessment Form.....	17
Appendix 2: Critical Appraisal Tool for Prevalence Studies.....	18
Appendix 3: Data Extraction Form for Prevalence Studies.....	19
Appendix 4: Online Survey Questionnaire	20

PART I: SYSTEMATIC REVIEW

1. BACKGROUND

1.1 Introduction

Trachoma is the leading infectious cause of blindness worldwide. It is caused by an intracellular bacterium *Chlamydia trachomatis* which is mainly transmitted through personal contact with infected persons as well as by flies that have been in contact with discharge from the eyes or nose of an infected person (World Health Organization, 2017a). In the early stages of infection, trachoma is often subclinical. However, repeated infection often leads to scarring of the tarsal conjunctiva which can lead to trichiasis (eyelashes touching the globe), an advanced stage of trachoma. Trichiasis presents a high risk for subsequent vision loss due to abrasion of the cornea (Taylor et al., 2014).

According to 2010 data, trachoma is responsible for the visual impairment of about 1.9 million people, of whom 0.45 million are irreversibly blind (Bourne et al., 2013). In addition, World Health Organization (WHO) estimates that, over 190 million people are currently at risk of trachoma blindness in the 41 endemic countries (World Health Organization, 2017a). Of these, 90.1% are from the WHO African region where conditions of very poor access to water and sanitation enhance transmission, with Ethiopia carrying the largest population at risk at 39% (World Health Organization, 2017b). Other populations affected by the disease include the poorest and most marginalized communities in Asia, Central and South America, Australia and the Middle East (World Health Organization, 2017a).

By itself, trachoma accounts for about 1.4% of all blindness worldwide (Bourne et al., 2013)(World Health Organization, 2017a). Mostly affecting the poor communities, the burden of blinding trachoma is huge in terms of the economic impact on individuals and communities. Overall, the economic cost in terms of lost productivity from blindness and visual impairment is estimated at US\$ 2.9 to 5.3 billion annually, increasing to US\$ 8 billion when trichiasis is included (Frick, Hanson & Jacobson, 2003).

In 1998, the World Health Assembly adopted a resolution (WHA51.11) aimed at eliminating trachoma as a public health problem (World Health Assembly, 1998). This resolution recommended use of the 1993 WHO trachoma elimination strategy denoted by the acronym “SAFE” which stands for: Surgery for people suffering from advanced stage of the disease i.e. trichiasis, Antibiotics to treat infection, Facial cleanliness and Environmental improvement to reduce transmission (World Health Organization, 2017a).

Since the adoption of the WHA51.11 resolution, significant progress has been made towards achieving the target goal of global elimination of trachoma by 2020 (GET2020). Today, over 30 countries are actively implementing the SAFE strategy and as a result of this, three countries have eliminated trachoma as a public health problem, namely; Oman, Morocco and Mexico (World Health

Organization, 2017b). A further seven countries have reported achieving the GET2020 elimination targets. These include Iran, China, Cambodia, China, Gambia, Ghana, Islamic Republic of Iran, Lao People's Democratic Republic, and Myanmar (World Health Organization, 2017b). As a result, the estimated number of people living in endemic districts, at risk of trachoma blindness, has declined from 317 million in 2010 to 190.2 million in 2016 (World Health Organization, 2017a,b).

1.2 Trichiasis Surgery

Surgery is an integral part of the SAFE strategy for trachoma elimination. The aim of surgery for trichiasis is to reduce the progression to corneal opacity and blindness which occurs as a result of repeated abrasion and ulceration of the cornea by in-turned eyelashes. Apart from improving ocular symptoms through correction of in-turned eyelids, surgery has also been shown to enhance patient comfort due to a decrease in photophobia and resolution of corneal swelling (Woreta et al., 2009).

There are numerous surgical and non-surgical procedures available for correcting trichiasis (Rajak, Collin & Burton, 2012). Surgical procedures generally involve a full thickness incision through the tarsal plate combined with several everting sutures to turn the distal part of the eyelid outwards (Yorston et al., 2006). The two most widely used surgical procedures for trichiasis are: Bilamellar tarsal rotation (BLTR) and Posterior Lamellar Tarsal Rotation (PLTR), also known as Trabut (West *et al.*, 2005). These two procedures have been recommended by WHO as the preferred surgical procedures for management of trachomatous trichiasis (World Health Organization, 2015).

According to results from various clinical trials, the two procedures have been found to yield better surgery outcomes, with low incidences of post-operative trichiasis at different follow up periods, compared to other surgical techniques (Reacher, Foster & Huber, 1993; Habtamu et al., 2016).

Further, both BLTR and Trabut have been found to require minimal surgical equipment and can be conducted in nearly any setting, thereby making them useful procedures in areas that do not have electricity or modern surgical facilities (Shannath, West & West, 2005).

1.3 Surgery outcomes and post-operative trichiasis

According to a recent systematic review on interventions for trichiasis (Burton *et al.*, 2015), there are various challenges involved in achieving good long-term surgical outcomes to prevent trachoma-related blindness. One of these is the high incidence of post-operative trichiasis following surgery reported in most programmatic settings, regardless of the intervention used (Burton et al., 2015).

Post-operative trichiasis is usually defined as the presence of one or more eyelashes touching the globe or evidence of epilation in an operated eye of a patient after surgery (Buchan, Limburg & Burton, 2011). This is broadly classified as either minor if fewer than five lashes are touching the globe or major if five or more lashes are touching the globe at any primary position (Khandekar, Mohammed & Courtright, 2001). Several factors have been associated with the post-operative

trichiasis after surgery among them; patient characteristics such as age and sex, preoperative disease severity, surgeon skills, surgical technique used and the post-operative environment (Burton et al., 2005).

Unfortunately, data on post-operative trichiasis is highly inconsistent due to differences in study design, type of surgical technique used and varying follow up periods (West *et al.*, 2005). According to (Burton et al., 2015), the average incidence of post-operative trichiasis in clinical trials is typically around 20% at one year post-surgery. However, evidence from other non-RCT studies on post-operative trichiasis have reported higher figures ranging from 10% at 3 months to over 60% at 3 years (Reacher et al., 1990, 1992; Shannath, West & West, 2005; West et al., 2005a; Rajak, Collin & Burton, 2012; Habtamu et al., 2016).

In addition, only limited operational data have been published from settings in which trachoma elimination programmes are active (Burton et al., 2015). Therefore, it is possible that under programmatic conditions, the cumulative incidence of post-operative trichiasis may be even higher. Without a proper understanding of the magnitude and determinants of post-operative trichiasis in the region, it is difficult to develop strategies to improve surgery outcomes for trichiasis, or even to determine how urgent their development might be.

This review aims to fill this gap by consolidating data from various published and unpublished studies on outcomes of trichiasis surgery with a focus on incidence and risk factors for post-operative trichiasis in Africa. The evidence will be useful in the planning and implementation of public health interventions to address post-operative trichiasis.

2. PURPOSE

2.1 Aim

The main aim of this systematic literature review is to assess post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa.

2.2 Objectives

1. To determine the incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa.
2. To compare the incidence of post-operative trichiasis and other poor outcomes in interventional studies and observational studies in Africa.

2.3. Review question

What is the prevalence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa?

3. METHODOLOGY

3.1 Search Strategy

A comprehensive search will be conducted to identify studies which have examined the outcomes of trichiasis surgery in Africa, with cumulative incidence of post-operative trichiasis as the primary outcome. The following electronic databases will be screened: PubMed, Academic Search Premier, Africa-Wide Information, CINAHL and Health Source Nursing through EBSCOhost, Web of Science [all databases], and Cochrane Central Register of Controlled Trials. In addition, Google scholar® and other relevant websites will be searched for grey materials. Reference lists of relevant reviews and all eligible papers will also be searched for related studies.

The search strategy for electronic databases will incorporate both Medical Subject Headings (MeSH terms) and free-text key terms which will be adapted to suit each individual database using applicable controlled vocabulary. The following MeSH terms and key terms will be used: ("Trichiasis"[Mesh] OR ("trichiasis"[MeSH Terms] OR "trichiasis"[All Fields])) OR ("Entropion"[Mesh] OR ("entropion"[MeSH Terms] OR "entropion"[All Fields])).

3.2 Inclusion and exclusion criteria

Types of studies

Randomised control trials (RCTs), controlled before-and-after studies (CBAs), prospective and retrospective cohort studies, case-control studies, case series, surveys and cross-sectional studies will be included in this review.

Study participants and condition

The study participants were: [a] for interventional studies: adults with un-operated trachomatous trichiasis or trachoma-related entropion of the upper lid in at least one eye or [b] for observational studies: adults with the presence of post-operative trachomatous trichiasis identified at the time of survey.

Primary outcome

Post-operative trichiasis defined as the presence of one or more eye lashes touching the globe after surgery.

Context

Only studies conducted in Africa will be included in the review.

3.3 Study selection

Two reviewers will screen titles and abstracts to select potential eligible studies. The full text of potentially eligible studies will then be obtained, and the final selection for inclusion into the review will be conducted by the two reviewers. Any disagreements regarding inclusion of studies will be resolved by discussion or by consulting a third reviewer if a consensus is not reached. A PRISMA flow diagram will be used to summarise the search and selection of studies for the review. A table of all studies included will be provided in the final review. The reasons for exclusion of studies will also be documented.

3.4 Quality assessment

The methodological quality of papers to include in the review will be assessed using a slight adaptation of the Joanna Briggs Institute critical appraisal checklist for prevalence studies (see appendix 2). Critical appraisal will be conducted by two reviewers independently of each other. The reviewers will then discuss the results of their critical appraisal for their final appraisal. Any disagreements will be resolved through discussion or by consulting a third reviewer if discussion fails to resolve the disagreement.

3.5 Data extraction

Data will be extracted from selected studies using the Joanna Briggs Institute standardised data extraction form (see appendix 3). Disagreements on study selection and data extraction will be resolved by consensus between the two review authors, failure to which a third author will arbitrate. Prior to use, the extraction form will be piloted on at least four studies identified randomly from the list of included studies.

3.6 Dealing with missing data

If necessary, we will contact the corresponding authors of included studies to give us any missing data. We will describe missing data for each included study and discuss the extent to which the missing data could alter our results.

3.7 Data synthesis

Quantitative data analysis and synthesis

Data on the incidence of post-operative trichiasis and other poor outcome of trichiasis surgery as reported in the primary studies will be expressed in proportions with the corresponding 95% confidence intervals for dichotomous data i.e. presence or absence of post-operative trichiasis. Where possible, similar studies will be grouped together to compare, broadly, similar types of outcome to get feasible results on an overall estimate of effect, mostly based on the follow-up period. The basic principles of the GRADE approach will be applied to the synthesis.

Subgroup analysis

Subgroup analyses will be conducted if possible, considering: study type (interventional study versus observational study), follow up period, and type of surgical technique used.

3.8 Discussion and reporting

This review will consolidate the available evidence on post-operative trichiasis in Africa. It is envisaged that the findings of this review will be used to inform efforts aimed at reducing post-operative trichiasis after surgery to enhance the achievement on WHO global target of eliminating trachoma by 2020. The systematic review findings will be disseminated in a peer-reviewed journal.

4. ETHICAL APPROVAL

The review will utilize findings of existing studies. In this case, no direct interaction with human subjects will be involved. Ethical approval for the study will be obtained from the University of Cape Town Health Sciences Research Committee and the WHO Ethics Review Committee.

PART II. ONLINE SURVEY

1. BACKGROUND

Post-operative trichiasis poses a major challenge to the current global efforts of eliminating trachoma by 2020. Unfortunately, its magnitude is likely to increase with increasing output of trichiasis surgery programmes in trachoma-endemic countries (World Health Organization, 2016a). According to West (2011), post-operative trichiasis undermines public confidence in trachoma control efforts and discourages patients from seeking surgery, thereby hampering efforts to eliminate trachoma by 2020. WHO recommends that all national trachoma elimination programmes should strive to achieve a 10% or less post-operative trichiasis at one year after surgery (World Health Organization, 2010). However, most studies conducted in trachoma endemic countries have reported significantly higher post-operative trichiasis ranging from 10% at 3 months to over 60% at 3-year follow up, with an average of 20% at one year follow up (Burton et al., 2005, 2015; Shannath, West & West, 2005; Gichangi et al., 2015).

To address this growing problem, WHO recommends regular monitoring of trichiasis surgery outcomes as a way of reducing post-operative trichiasis (Courtright, Burton & Emerson, 2012). In this case, it is recommended that every trachoma programme should have a system for detecting and managing post-operative trichiasis through proper patient follow up at least 6 months after surgery and recording of surgical outcomes at every follow up (World Health Organization, 2014; Merbs et al., 2015). In addition, follow-up data on any confirmed cases of post-operative trichiasis should also be systematically collected and collated. For quality assurance purposes, surgical audits of surgeons are recommended and if a surgeon's patients are found to have an unusually high incidence of post-operative trichiasis, enhanced supportive supervision by a more experienced surgeon, or re-training, may be needed (Courtright, Burton & Emerson, 2012; Merbs et al., 2015).

Unfortunately, many countries have yet to put in place policies and systems to track and monitor outcomes of trichiasis surgery (World Health Organization, 2016b). This online survey aims to assess the availability of national policies and strategies for monitoring outcomes and conducting surgical audits, and strategies for addressing poor surgical quality among surgeons as well as evaluate the targets for good trichiasis surgical outcome in 29 African countries where trachoma is still considered a public health problem.

2. PURPOSE

2.1 Aim

The purpose of this survey is to assess the current national targets for good surgical outcomes, national policies and strategies for monitoring outcomes and conducting surgical audits, and strategies for addressing poor surgical quality among surgeons.

2.2 Objectives

1. To identify national targets for good surgical outcome (% of patients with no post-operative trichiasis).
2. To identify and document the national policies and strategies to monitor surgical outcomes and conduct surgical audits.
3. To identify national strategies for addressing poor surgical quality among surgeons.

3. METHODOLOGY

3.1 Study design

This will be a cross-sectional survey conducted using an online questionnaire which will be administered to all national trachoma programme coordinators via email.

3.2 Study setting

The survey will be conducted in the 29 African countries where trachoma is still considered a public health problem.

3.3 Inclusion and exclusion criteria

All national coordinators for trachoma control programmes in the 29 trachoma-endemic countries in the WHO African Region will be included in the survey.

3.4 Recruitment of participants

Participants will be recruited via email sent to all national coordinators of trachoma programmes in Africa. Only those who consent to participate will be sent the questionnaire.

3.5 Data collection

An online survey questionnaire will be used to collect information on targets for surgical outcomes, policies and monitoring, and strategies to address poor performance by surgeons. The questionnaire will be translated into French and Portuguese for non-English speaking countries.

3.6 Data entry and analysis

Data will be entered into Microsoft Excel for cleaning and analysis. Absolute and relative number of responses will be determined for each question, providing counts and percentages, respectively. Aggregated tables, as well as pie and column charts will be generated to represent results. Qualitative data will be analysed using thematic analysis and narrative synthesis.

4. ETHICAL APPROVAL

Ethical approval for the study will be obtained from the University of Cape Town Health Sciences Research Committee and the WHO Ethics Review Committee.

4.1 Informed consent

Before commencing the survey, electronic consent will be obtained from every participant, after explaining the purpose of the research, the nature of their requested participation, and an opportunity to ask questions. Participation will be completely voluntary, and the participants will be informed of their alternatives to participation, including their right to refuse or withdraw participation at any time during the study without penalty.

4.2 Privacy and confidentiality

Throughout the survey, anonymity, privacy and confidentiality of the information gathered will be emphasised and upheld. Data collected during this study will be stored electronically on two separate password-protected computers. Any information that is obtained in this study that can be identified will remain confidential and will only be disclosed with the participant's consent or as required by law. If the results of the study are published, no names or identifying characteristics will be mentioned, except where consent to do so has been obtained.

4.3 Potential risk and benefits

Since the survey will be collecting operational data, it poses minimal risk to the participants and the trachoma control programmes. Data obtained from the survey will be useful in developed strategies to reduce post-operative trichiasis in Africa.

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LIST OF APPENDICES

Appendix 1: Study Eligibility Assessment Form

Study Eligibility Assessment Form

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Study characteristics (Compare against the eligibility criteria as defined in the Protocol)	Eligibility criteria met?			Location in text or source (page #/fig/table/other)
		Yes	No	Unclear	
Type of study	Randomised Controlled Trial	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Controlled Before and After Study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Cohort study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Case-control study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Cross-sectional study/survey	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Other design (specify):	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Study Participants		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Type(s) of intervention		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Primary outcome		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Secondary outcomes		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Study setting/context		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Overall appraisal: Include <input type="checkbox"/> Excluded <input type="checkbox"/> Seek further info <input type="checkbox"/>					
Reason for exclusion					
Additional Notes:					

Appendix 2: Critical Appraisal Tool for Prevalence Studies



JBI CRITICAL APPRAISAL CHECKLIST FOR STUDIES REPORTING PREVALENCE DATA

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Was the sample frame appropriate to address the target population?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were study participants sampled in an appropriate way? (if an RCT, was randomisation done correctly?)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the sample size adequate?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were the study subjects and the setting described in detail?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Was the condition of interest (post-operative trichiasis) measured as one of the primary outcomes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were valid methods used for the identification of the condition?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Was the condition measured in a standard, reliable way for all participants?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was there appropriate statistical analysis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Was the follow rate adequate, and if not, was the low response rate managed appropriately?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Addition comments (Including reason for exclusion)

Appendix 3: Data Extraction Form for Prevalence Studies



JBI DATA EXTRACTION FORM FOR INTERVENTIONAL STUDIES

Reviewer's Name –
Study ID/Record Number -
Date –
Study details
Study title –
Author –
Year –
Journal –
Aims of the study:
Study Method
Setting –
Study design –
Sample Size –
Subject characteristics –
Intervention group –
Control group -
Follow-up or study duration –
Loss to follow up -
Primary Outcome –
Other outcomes:
Outcome measurements –
Method of data analysis –

Appendix 4: Online Survey Questionnaire

Dear Participant,

You are invited to participate in this survey to assess the current national targets for good trichiasis surgical outcomes, national policies and strategies for monitoring outcomes and conducting surgical audits, and strategies for addressing poor surgical quality (where identified) in trachoma endemic countries in Africa. Your participation is voluntary – but we would really like you to take part! The information that you could provide will help the global trachoma elimination programme to refine approaches for optimising surgical outcomes internationally.

The survey procedure involves just responding to the questionnaire below. It is expected that this might take you up to 30 minutes to complete.

If you are willing to take part, please answer all questions as accurately as possible by ticking the appropriate box or writing your response in the blank space provided. All responses are confidential, and all data will be compiled without identification of the respondent or the country. Data collected during the survey will be stored electronically on a password-protected computer.

The survey findings will be used as a foundation to discuss additional strategies to reduce post-operative trichiasis. If the results of the survey are published, no responses will be attributed to you or your programme, and any identifying characteristics of your programme that you provide in your responses will be removed. By returning this form you are providing consent for the information to be included in the survey.

Kindly return the completed questionnaire to mwngra003@myuct.ac.za. If you have any questions about the study, please do not hesitate to contact me, Professor Paul Courtright (pcourtright@kcco.net) or Dr Anthony Solomon (solomona@who.int).

Thank you very much in advance for your participation!

ELECTRONIC CONSENT

I have read and understood the nature and purpose of this study and I voluntarily agree to participate.

Yes

No

Full Name: Click or tap here to enter text.

Designation/ Job title: Click or tap here to enter text.

Country: Choose an item.

Date: Click or tap to enter a date.

SURVEY QUESTIONS

Q.1. What is the national target for good trichiasis surgery outcomes in your country? (that is, what does your health ministry set as the minimum % of trichiasis surgeries that should achieve a good outcome [absence of post-operative trichiasis, or some other definition] at 3-6 months after surgery, or at the last routine follow-up period?)

Click or tap here to enter text.

Q.2. Is there a written national policy for the timing of follow-up and outcome assessment after trichiasis surgery (time periods when patients are expected to be seen again after surgery)?

- Yes (*Please attach*)
- No written policy, and no expectation for outcome assessment
- No written policy, but surgeons are expected to follow up and assess outcomes on their trichiasis cases
- No written policy, but the country has adopted ICTC preferred practice guidelines
- Other. *Please specify.* Click or tap here to enter text.

Q.3. At what time periods after trichiasis surgery is it recommended (as national policy or otherwise) for a trichiasis patient to have a follow up examination in your country? (*Please tick all the follow up periods that apply*)

- 1-day after surgery
- 1-2 weeks after surgery
- 3-6 months after surgery
- 1 year after surgery
- Other. *Please specify.* Click or tap here to enter text.

PART A: STUDY PROTOCOL

Q.4 Is there a written national policy for conducting audits of trichiasis surgeons in your country? (Here, an audit refers to an assessment of the surgical outcomes of patients operated on by a surgeon or group of surgeons, with the assessment undertaken by a supervisor or other independent person.)

- Yes (*Please attach*)
- No written policy, but the health ministry has adopted other guidelines, e.g., the Queen Elizabeth Diamond Jubilee Trust-funded surgical audit guidelines (*Please attach*)
- No written policy, and no agreed approach to conducting audits
- No written policy, but audits of trichiasis surgeons are undertaken by supervisors
- Other. *Please specify.* Click or tap here to enter text.

Q.5. In your country, is there an accepted maximum incidence of post-operative trichiasis in a surgeon's patients, above which a surgeon is asked to discontinue surgery until retraining or other interventions have been undertaken?

- Yes. *Please state the cut-off point in %* Click or tap here to enter text.
- No

Q.6. What is the current standard of care for managing post-operative trichiasis in your country (please tick/list all approaches that are deemed by the health ministry to be acceptable)

- Management by a specially-trained ophthalmologist (e.g., an oculoplastic surgeon)
- Management by any ophthalmologist
- Management by another trichiasis surgeon
- Management by the surgeon who did the first procedure
- Other approaches. *Please specify.* Click or tap here to enter text.

PART A: STUDY PROTOCOL

Q.7 What challenges have you faced in managing post-operative trichiasis in your country? (*Please list all challenges*)

Click or tap here to enter text.

Q.8. What other strategies would you recommend for reducing the incidence of post-operative trichiasis in your country? (*Please list all strategies*)

Click or tap here to enter text.

~END~

Thank you for taking part in the survey.

PART B: LITERATURE REVIEW

TABLE OF CONTENTS

1. BACKGROUND 2

1.1 Description of the condition..... 2

1.2 Global Distribution and Burden..... 2

2. TRACHOMATOUS TRICHIASIS 3

2.1 Interventions for trichiasis 4

2.2 Outcomes of TT surgery 7

2.3 Post-operative trichiasis 7

2.4 Strategies to address post-operative trichiasis 11

REFERENCES 14

List of Figures

Figure 1. Bilamellar tarsal rotation: 5

Figure 2. Posterior lamellar tarsal rotation..... 6

1. BACKGROUND

1.1 Description of the condition

Trachoma is the leading infectious cause of blindness globally (Taylor et al., 2014). It is a known public health problem in 41 countries (World Health Organization, 2017) and is responsible for the blindness or visual impairment of about 1.9 million people (World Health Organization, 2018a). According to WHO Weekly Epidemiological Record released in June 2018, 157.7 million people currently live in trachoma endemic areas and are at risk of trachoma blindness (World Health Organization, 2018b). In 2017, over 70 million people were living in the trachoma endemic areas of Ethiopia – accounting for over 44% of the global burden of active trachoma. Women are 1.8 times as likely to have trichiasis compared to men as a result of repeated trachoma infections due to their role as traditional caretakers of children, who often are the primary hosts for the disease in their communities (Cromwell et al., 2009).

In trachoma-endemic areas, active trachoma is common among preschool-age children (World Health Organization, 2018c). With increasing age, the re-infection becomes less frequent and shorter in duration. However, in endemic communities, re-transmission of the organism occurs frequently through direct contact with eye and nose discharges from infected individuals, by contact with fomites or/and flies. Active trachoma can be treated using antibiotics.

Repeated trachoma infections may lead to severe scarring of conjunctival causing it to turn inwards and the eyelashes to rub against the eyeball. This condition is known as trachomatous trichiasis. Some of the common symptoms associated with this stage of trachoma include; photophobia, pain and in turned eyelashes which often lead to scarring of the cornea (Rajak, Collin & Burton, 2012). Left untreated, trachomatous trichiasis can result in the formation of corneal opacities which may lead to irreversible blindness.

1.2 Global Distribution and Burden

Trachoma predominantly affects poorest communities of Sub-Saharan Africa, the Middle East, and Asia (Burton & Mabey, 2009). As such, the economic impact of blinding trachoma on individuals and communities is high since the communities are already poor. According to (Frick, Hanson & Jacobson, 2003), the economic cost of trachoma-related visual impairment is estimated at US\$ 5.3 billion per year with an annual productivity loss of up to US\$8 billion when trichiasis is included.

In 2009, over 50 countries were trachoma-endemic and approximately 41 million people had active trachoma (Mariotti, Pascolini & Rose-Nussbaumer, 2009). As of June 2018, the number of trachoma endemic countries stood at 43 with 7 countries having been validated for elimination by WHO since 2012. These are: Oman in 2012, Morocco in 2016, Cambodia, Mexico and Lao People's Democratic Republic in 2017, and Ghana and Nepal in 2018 (World Health Organization, 2018a). In addition, the

estimated number of people at risk of trachoma blindness has declined from 317 million in 2010 to 157.7 million in 2018. This decline is probably due to the success of the 'AFE' components of SAFE strategy implemented through the national trachoma control programs in various countries, more accurate disease estimates, and economic development in some trachoma endemic areas (World Health Organization, 2016a).

In 2017, over 231,000 people received surgery for trichiasis and 83.5 million people received antibiotics for active trachoma - reaching a first time high of over 50% global-level of antibiotic coverage (World Health Organization, 2018b). A recent estimate places the burden of trichiasis at around 2.8 million people down from 8.2 million cases in 2007 (Flueckiger et al., 2018).

2. TRACHOMATOUS TRICHIASIS

Trachoma mostly occurs in early childhood as a result of *C. trachomatis* infection of the conjunctival epithelium which provokes a follicular conjunctivitis. This stage is known as active trachoma and is characterized by an inflammatory cell infiltrate and a pro-inflammatory cytokine response (el-Asrar et al., 1989; Burton et al., 2004). In endemic communities, repeated infections are likely to occur due to presence of enabling environmental factors such as poor hygiene, overcrowding, water shortage and poor sanitation. These repeated infections may cause chronic inflammation leading to scarring of the tarsal plate and conjunctiva of the inside of the eyelid. If left untreated, this leads to turning of the eyelid margin inward, also known as cicatricial entropion, and may be severe enough to turn the eyelashes inwards causing trichomatous trichiasis which is the blinding stage of trachoma (Burton et al., 2004).

Eventually, the continuous corneal abrading by in turned eye lashes and secondary microbial keratitis causes corneal opacification leading to loss of vision. Blindness resulting from trachoma is both painful and irreversible. Although keratoplasty may be used to treat corneal scarring due to trachoma, it is rarely available due to lack of donor corneas and the risk of failure is high, especially in trachoma-endemic countries (Yorston, Wood & Foster, 1996).

It is important to note that, not all trichiasis is due to trachoma. Chronic blepharitis, viral conjunctivitis, ocular cicatricial pemphigoid, Steven-Johnson syndrome, erythema multiforme, distichiasis, trauma, chemical injury, and surgical procedures can also cause eyelashes to touch the eye (Khafagy, Mostafa & Fooshan, 2012). This is referred to as non-trichomatous trichiasis. Currently, the prevalence of non-trichomatous trichiasis is not known for either non-trachoma endemic areas or trachoma-endemic areas (World Health Organization Strategic and Technical Advisory Group on Neglected Tropical Diseases, 2015). In this study, we only focused on trichomatous trichiasis, which is the result of multiple infections with *C. trachomatis*.

2.1 Interventions for trichiasis

Trachoma has been in existence since ancient times and so has its treatments. The Ebers Papyrus, an Egyptian medical collection of herbal knowledge dating back to circa 1550 BC (Ebbell, 1937), has documented over 70 prescriptions that were used to treat trachoma and other eye diseases in ancient Egypt. Much of this treatment was based on topical medicines drawn from animal, vegetable and mineral products such as myrrh, lizard or bat's blood, often applied to the infected eye using a vulture's feather (Taylor, 2008). In ancient Greece (4th Century BC), however, topical treatments were not preferred; instead, treatments to divert inflammation from the infected eye to other parts of the body were used. Up until this point, the only available treatment for trichiasis was pulling out the in-turned lashes to reduce discomfort.

In circa 1000--500 BCE, the use of cautery, lid incision and everting sutures for entropion and trichiasis were reported in India (Taylor, 2008). During the Roman Empire, surgery for trichiasis became more common. It involved eyelash epilation and lash follicle cautery with a hot iron, which has parallels to modern lash-root cautery procedures. In the 5th century, more treatments started to emerge with the introduction of three types of operations to treat trachoma namely; the scarification of the granular conjunctiva followed by the application of copper compounds; surgical excision of the granular tissue followed by lash follicle cautery with a hot iron; and eyelash epilation to correct entropion and trichiasis (Taylor, 2008). These principles were adopted by Greek and Roman practitioners and formed the basis of trachoma treatment until the introduction of modern medicine – antibiotics- in 1937.

In the 7th century CE, Paul of Aegina wrote a major medical compendium drawing on the medical knowledge of Hellenistic Alexandria and the Roman physicians. He described the treatment of trichiasis by removing a piece of eyelid skin by clamping a fold of skin between two pieces of reed. This technique produces a degree of lid eversion and was still used by traditional healers in Myanmar in the 1970s (Win, 1976). Trichiasis treatment remained essentially unchanged from ancient times until the 19th century, when new oculoplastic procedures started to be developed for entropion.

Over the past century, many surgical and non-surgical procedures for the treatment of trichiasis have emerged. These treatment options can be divided into two broad categories – lash treatments and corrective lid surgery. Lash treatments are aimed at treating the in-turned lashes to reduce the risk of cornea opacification and they include epilation, lash follicle destruction procedures such as cryotherapy, electrolysis, argon laser photocoagulation and radiotherapy, and surgical excision of aberrant lash-bearing follicles or tissue (Rajak, Collin & Burton, 2012). Corrective eyelid surgery, on the other hand, refers to those surgical techniques which are aimed at correcting the underlying eyelid abnormality by mobilizing the entropic component of the eyelid, then repositioning and placing a suture to prevent the eyelashes from scratching the cornea.

The purpose of the surgery is to correct the entropion and trichiasis by rotating the eyelid margin outward, directing the eyelashes away from the globe. Tarsal rotation procedures - Bilamellar Tarsal Rotation (BLTR) and Posterior Lamellar Tarsal Rotation (PLTR) also known as Trabut - are the most widely used surgical procedures in trachoma endemic regions (Merbs *et al.*, 2015) and have been recommended for trachomatous trichiasis by WHO due to their better outcomes compared to other surgery techniques.

2.1.1 Bilamellar Tarsal Rotation

The WHO trichiasis surgery manual WHO/PBL/93.29 published in 1993 recommended BLTR as the preferred procedure for correcting trichiasis (Reacher, Foster & Huber, 1993). In this procedure, the eyelid is fixed by placing a haemostat at the medial end of the upper lid lateral to the lachrymal punctum and another at the lateral end of the upper lid extending 5mm in from the lid margin (Reacher, Foster & Huber, 1993). Thereafter, an incision is made through all the skin at 3mm above and parallel to the lid margin for a length of about 20 mm (Reacher *et al.*, 1990). This incision should be made in two stages: first through the anterior lamella and second, after everting the lid, through the posterior lamella to meet the first (Reacher, Foster & Huber, 1993). Sutures are then inserted running from the tarsal conjunctiva to the anterior lamella component of the distal fragment to rotate the lid margin outwards and ensure that the eyelashes are no longer in contact with the cornea (Reacher, Foster & Huber, 1993). Silk sutures are the most widely used and must be removed at 7--10 days postoperatively (Rajak, Collin & Burton, 2012). Finally, the external wound is closed with two or three skin sutures to complete the surgery (Figure. 1).

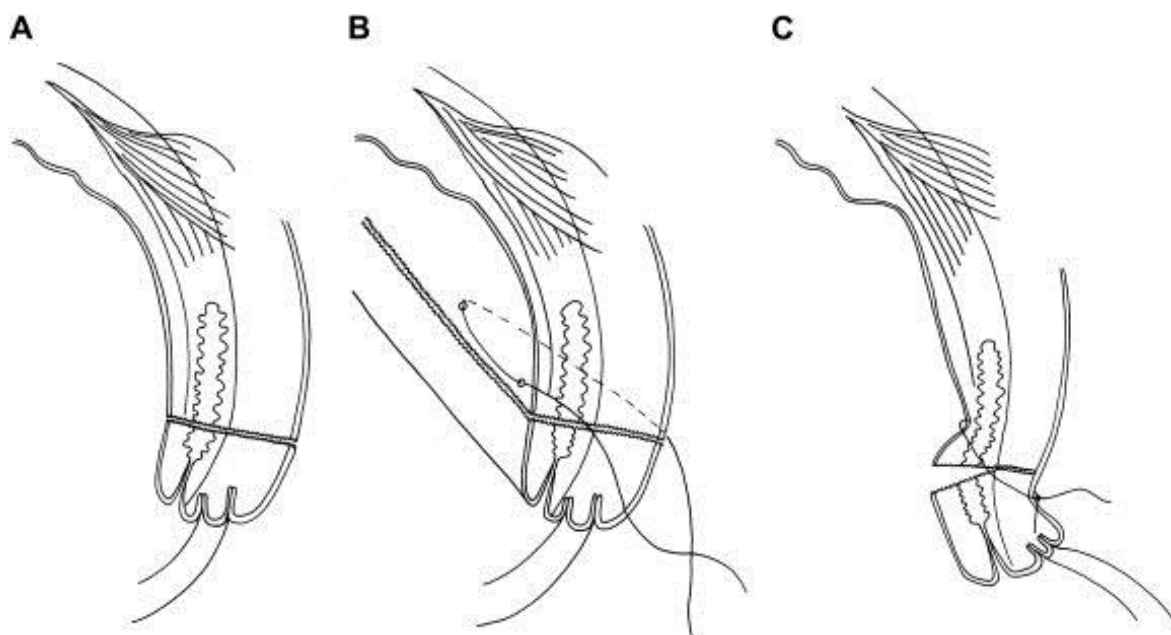


Figure 1. Bilamellar tarsal rotation surgery technique: A: Bilamellar incision. B: Horizontal mattress suture. C: Postoperative lid eversion (Rajak, Collin & Burton, 2012).

2.1.2 Posterior Lamellar Tarsal Rotation

PLTR refers to several operations that combine tarsotomy with everting sutures (Rajak, Collin & Burton, 2012). The PLTR procedures vary in their degree of dissection of the anterior and posterior lamellae and in the positioning of the everting sutures. In Trabut, which is one of the PLTR procedures, eyelid is fixed on the Trabut plate, incised through the posterior lamella (conjunctiva and tarsal plate) 3mm above and parallel to the eyelid margin, and stopping at the orbicularis muscle (World Health Organization, 2015). The muscle is then dissected from the tarsal plate in both fragments until the dark bulbs of the lash follicles just become visible (Rajak, Collin & Burton, 2012). Three horizontal everting mattress sutures are then used to suture the fragments so that the eyelid margin is rotated outwards and the eyelashes no longer touch the globe (Fig. 4). As the sutures are tightened the proximal segment of the posterior lamella is drawn down and tucks in behind the distal segment of the posterior lamella and the lid everts (Merbs *et al.*, 2015).

There are various variations of the PLTR including continuous sutures, mixture of continuous and mattress sutures, rubber bolsters to tie sutures over, combining PLTR with a tarsal and/or dis-insertion of Müller's muscle, and combining posterior tarsal fracture with a shallow gray line split (Rajak, Collin & Burton, 2012).

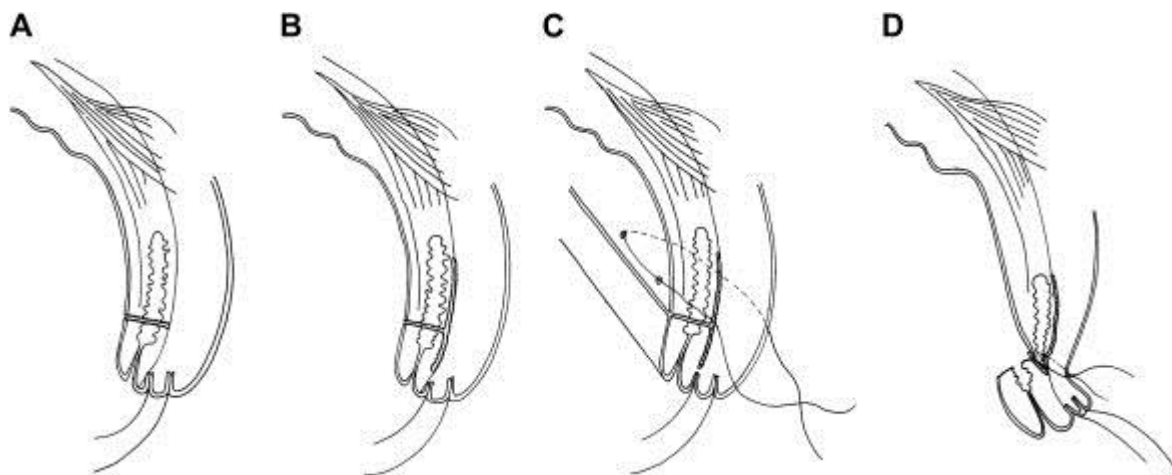


Figure 2. Posterior lamellar tarsal rotation technique. A: Posterior lamellar incision. B: Dividing anterior and posterior lamellae. C: Horizontal mattress sutures. D: Postoperative lid eversion (Rajak, Collin & Burton, 2012).

2.1.3 Other corrective lid surgery procedures

These include Tarsal Advance, Tarsal Advance and Rotation, Anterior Lamellar Repositioning, Eversion Sprinting and Lid Margin Procedures, Tarsal Grooving also known as Anterior Tarsotomy, and Tarsectomy (Rajak, Collin & Burton, 2012).

2.2 Outcomes of TT surgery

Surgery is an integral part of the WHO SAFE strategy for prevention of trachoma-related blindness (Reacher, 1992). However, not all TT patients require surgery; if a patient has only one or two misdirected lashes with no corneal complications, repeated epilation or other lash treatments may be sufficient to reduce discomfort and prevent cornea scarring. But if there are one or more in turned lashed which are scratching the cornea or evidence of corneal damage, this is a definite indication for surgery (Reacher, Foster & Huber, 1993). Further, if the patient has defective lid closure, tarsal rotation surgery is recommended (Reacher, Foster & Huber, 1993).

The high prevalence of TT, huge backlog of trichiasis cases and the limited surgical services in most endemic countries demands a simple, quick procedure that can be taught to and carried out by non-ophthalmologists with the most basic equipment in the most basic settings (World Health Organization, 2006). A randomized controlled trial comparing the outcome of BLTR surgery conducted by ophthalmologists versus Integrated Eye Care Workers found that there was no statistically significant difference in the outcomes, especially in the incidence of post-operative TT recorded in the two groups (Alemayehu et al., 2004).

The second edition of *Trichiasis surgery for trachoma* (World Health Organization, 2015), recommends the use of either BLTR and the PLTR Trabut procedure for the treatment of trichiasis. Even though these are considered the best, practical procedures, they have been found to yield favourable outcomes at intervals after surgery on an imperfect proportion of patients; this undermines efforts to eliminate trachoma. Poor post-surgical outcomes affect both the individual and the trachoma control program as a whole (Habtamu et al., 2017). In addition to post-operative trichiasis, some of the most common poor outcomes reported after TT surgery include surgical complications such as granulomas, lid notching, over correction and wound infection, poor visual acuity and corneal opacity (Rajak et al., 2011; Habtamu et al., 2016). These poor outcomes have been attributed to various factors broadly categorized into two; surgery and surgeon-related factors such as the surgery technique used, type of suture materials used and surgeon's skills and experience among others, and patient-specific factors such as the severity of the pre-operative disease, presence of active *C. trachomatis* infection, duration since surgery, age and gender among others (Rajak, Collin & Burton, 2012).

2.3 Post-operative trichiasis

Post-operative trichiasis is often defined as the presence of one or more eyelashes touching the globe or evidence of epilation in an operated eye of a patient after surgery (Buchan, Limburg & Burton, 2011). It can develop at any time after surgery putting the eye at a renewed risk of sight loss. Early post-operative trichiasis which develops within the first six months after surgery is often related to how well the operation was performed, or to the patient's wound healing responses.

The proportion of eyes that develop post-operative trichiasis is variable ranging from 10% at 3 months to 62% at 3 years (Reacher et al., 1992, 1990; Reacher, 1992; Bowman et al., 2000; R Khandekar, A. J. Mohammed and Courtright, 2001; Khandekar, Mohammed and Courtright, 2001; Burton et al., 2005; Shannath, West and West, 2005; West et al., 2005; Rajak et al., 2011; Gower et al., 2013; Esmael Habtamu et al., 2016; Habtamu et al., 2017, Burton et al., 2005, 2015; Gichangi et al., 2015). Generally, the incidence of post-operative trichiasis reported in clinical trials is typically around 20% one year after surgery. However, numbers reported in observational studies and the cumulative incidence over the years are much higher. Inconsistencies in the follow-up periods and lack of operational data from settings in which trachoma elimination programmes are active has made it difficult to reliably estimate and compare the incidence of post-operative trichiasis but overall, there appears to be a consistent pattern of high incidence of post-operative trichiasis. It is possible that under programmatic conditions, the incidence of post-operative trichiasis and other poor outcomes is even higher and therefore must be monitored.

A wide range of preoperative, intraoperative and immediate postoperative factors have been attributed to this high incidence of post-operative trichiasis. These include surgery procedure, surgical factors such as the length of incision, distance of the incision from the lid margin, peripheral dissections and attention to suturing, post-operative care including the use of azithromycin after surgery, surgeon's handedness, skills and experience and patient-specific factors such as severe preoperative trichiasis, active bacterial infection, and severe conjunctival inflammation (Taylor, 2008). Although some of these factors such as pre-operative disease severity and surgeon's skills, experience and their attention to technique have repeatedly been shown to affect the surgical outcomes (Taylor, 2008), others still require further investigation.

A study conducted by (West et al., 2005) in a trachoma-endemic area of central Tanzania concluded that, post-operative trichiasis after surgery was associated with the technique, skill, and experience of the surgeon. The study found a high incidence of post-operative trichiasis (28%) at 18 months after surgery and although the researchers could not specifically evaluate the surgeons' skill and technique, the district-specific incidence (16% to 18%) showed significant differences in districts that had regular refresher surgeon training compared to those that did not have refresher training. Similarly, in a trachoma control program in Northern Nigeria, it was noted that there were more cases of early-onset post-operative trichiasis occurring within the first 3 months of surgery among some surgeons. This was attributed to declining skills of the surgeons which had led to poor attention to surgical details like forceps placement on lid, height of incision and suture placement, thereby resulting in inferior quality surgeries and a high incidence of post-operative trichiasis (Rabiu, Muhammed & Isiyaku, 2011). With refresher training, the quality of surgery improved significantly with good lid rotation and less incidence of early post-operative trichiasis (Rabiu, Muhammed & Isiyaku, 2011).

In terms of the surgical procedure, BLTR and PLTR have been found to produce better outcomes compared to other procedures in the treatment of TT. A non-concurrent prospective study conducted in Oman (Khandekar, Mohammed and Courtright, 2001) to compare the incidence of long-term post-operative trichiasis following tarsal rotation and electro-epilation procedures (n=603) found that, after an average follow up period of 3.1 years, there was a post-operative trichiasis incidence of 61.8% among patients who had undergone tarsal rotation patients and 50.6% among patients who had undergone electro-epilation patients. Severe post-operative trichiasis was also detected among 27% of tarsal rotation patients and 10% of electro-epilation patients (Khandekar, Mohammed and Courtright, 2001). In this study, the high incidence of post-operative trichiasis was found to be associated with female gender, residence in a high-risk region and time since surgery. A randomised controlled non-inferiority trial conducted in Ethiopia to compare the surgery versus epilation for the treatment of minor trichiasis (n=1300) was inconclusive regarding inferiority of epilation to surgery for the treatment of minor trichiasis, relative to the pre-specified margin after a follow up period of 24 months. According to the findings of this trial, epilation had a comparable effect to surgery on visual acuity and corneal outcomes with a cumulative risk of post-operative trichiasis of 13.2% in the epilation group and 2.2% in the surgical group (Rajak et al., 2011).

Another randomized controlled trial comparing BLTR and Transverse Tarsotomy and lid margin Rotation conducted in Ethiopia (n=153) reported that, after a 3-month follow up period, there was no statistically significant difference in the incidence of post-operative trichiasis between BLTR and Transverse Tarsotomy and lid margin Rotation ($P = 0.711$). However, complications such as lid-notching and granuloma were observed more in BLTR than in Transverse Tarsotomy and lid margin Rotation group and this was statistically significant ($P = 0.002$) (Adamu & Alemayehu, 2002).

Other comparative trials have been conducted to compare the two tarsal rotation procedures in terms of their surgical outcomes (Habtamu *et al.*, 2016). However, most of these have failed to demonstrate a statistically significant difference in the incidence of post-operative trichiasis between patients undergoing BLTR and PLTR. According to a study conducted in 1986 in Oman (n=165) to compare the success rate of five procedures – BLTR, tarsal advance and rotation (modified Trabut), eversion splinting (grey line), tarsal advance (lid split), and tarsal grooving (Streatfield-Snellen) procedures, BLTR was significantly more successful than eversion splinting; tarsal advance and tarsal grooving but not significantly more successful than tarsal advance and rotation (Reacher et al., 1990). Another controlled trial conducted in Oman (n= 67 patients) showed a significantly higher risk of post-operative trichiasis in patients who received tarsal advance and rotation than in those who received BLTR at 21 months post-surgery (Reacher et al., 1992). However, it is important to note that in these studies, a variant of PLTR employed differed in technique to the Trabut procedure currently advocated by WHO (World Health Organization, 2015).

In a more recent randomised, controlled, single masked clinical trial conducted in Ethiopia (n=1000) (Habtamu et al., 2016), the cumulative incidence of post-operative trichiasis at the 12-month follow up assessment was more frequent in the BLTR group (22%) than in the PLTR group (13%), the difference being statistically significant. In this case, PLTR surgery was found to be superior to BLTR surgery for management of trachomatous trichiasis (Habtamu *et al.*, 2016).

On the surgical technique, a study by (Habtamu et al., 2017) found that, the length of the incision medially and laterally markedly reduced the rate of post-operative trichiasis for both PLTR and BLTR. A longer incision allows the distal segment to rotate adequately, and once secured with sutures, it is less likely to revert to the original entropic position. In addition, the study found lower incidence of post-operative trichiasis in cases with an incision height of ≥ 4 mm from the lid margin in PLTR surgery. These findings are comparable to those reported in two other studies conducted in Tanzania (Merbs, West & West, 2005; Merbs, Oktavec, et al., 2015). In the first study which sought to examine the role of the surgical technique in post-operative trichiasis after BLTR surgery, post-operative trichiasis was found to be more common in the left eye than in the right eye thereby suggesting a contribution of surgical technique to occurrence of post-operative trichiasis (Merbs, West & West, 2005). In this case, it was concluded that since it was more difficult for right-handed surgeons to operate on the right eye, it is likely that the surgeons unintentionally modified the surgical technique when operating on the right eye with a greater propensity to cut closer to the margin than 3 mm when extending the incision to the right. This unintended modification with potential tendency to cut closer to the margin on the right side of the eyelid may correspond to better surgical outcomes on the right eye (Merbs, West & West, 2005). In the second study, an internal scar height < 4.5 mm measured 1 year after surgery was found to be associated with post-operative trichiasis (Merbs, Oktavec, et al., 2015).

In view of plausible linkage between post-operative trichiasis and recurrent infections or intensity of active infections, the use of perioperative azithromycin has been encouraged. However, the effect of such perioperative antibiotics in reducing the incidence of post-operative trichiasis is yet to be conclusively established. A randomised controlled trial conducted in the Gambia (Burton et al., 2005) to assess whether azithromycin can improve surgical outcomes (n=451) found that, azithromycin did not improve the outcome of trichiasis surgery. The incidence figures in this study stood at 41.3% minor trichiasis and 19.7% major trichiasis at 1 year. However, a separate study conducted in Ethiopia (n=1452) found that, a single dose of azithromycin can reduce the incidence of severe post-operative trichiasis at one year, with relative risk of 4.2/100 person years among patients who received azithromycin compared to 7.9/100 person years among patients randomized to receive topical tetracycline ($P < 0.01$) (West et al., 2007).

More recently, a randomised, double-blind, placebo-controlled trial conducted to investigate the role of oral doxycycline in preventing postoperative trichomatous trichiasis in Ethiopia (n=1000) found that, after 12 months follow up period, doxycycline did not reduce the risk of postoperative trichiasis and is therefore not indicated for the improvement of outcomes following trichomatous trichiasis surgery (Habtamu et al., 2018).

2.4 Strategies to address post-operative trichiasis

Post-operative trichiasis is a significant problem and its magnitude is likely to increase with increasing output of trichiasis surgery programmes in trachoma-endemic countries (World Health Organization, 2016a). Preliminary analysis of population-based data from the Global Trachoma Mapping Project indicates that, 10-75% of people who currently have trichiasis have already had trichiasis surgery before (World Health Organization, 2016a). This undermines progress towards eliminating trachoma, thus necessitating urgent measures to reduce poor outcomes and specifically, post-operative trichiasis.

WHO recommends regular monitoring of trichiasis surgery outcomes as a way of reducing post-operative trichiasis (Courtright, Burton & Emerson, 2012). According to the *Trachoma Control: A Guide for Programme Managers* (World Health Organization, 2006), all operated trichiasis patients should be seen on the first post-operative day for eye patch removal and examination of the wound. A follow-up assessment should be done 8 to 14 days at which point the patient's visual acuity should be measured, and sutures removed, that is if non-absorbable sutures were used. If infection is suspected, the patient should be provided with a course of antibiotics to manage it and if the patient is found to have a granuloma around a stitch or in the wound, this should be removed under local anaesthesia. Further follow-up should be done at 6 months after surgery (World Health Organization, 2016a) and/or at one year (World Health Organization, 2006). During every follow-up visit, the visual acuity should be measured, and both eyes examined for presence of post-operative trichiasis in the operated eye or new TT in an unoperated eye. In addition, follow-up data on any confirmed case of post-operative trichiasis should also be systematically collected and collated.

For quality assurance purposes, surgical audits of surgeons are recommended. According to a report of the WHO GET2020 second Global scientific meeting held in 2015, programmes should review the performance of new trichiasis surgeons 3 to 6 months after certification, and of existing trichiasis surgeons' performance at least annually (World Health Organization, 2016a). If a surgeon is found to have unacceptably high incidence of post-operative trichiasis and other poor outcomes above the pre-determined threshold, re-training and supportive supervision by a more experienced surgeon may be needed (Buchan, Limburg & Burton, 2011; Courtright, Burton & Emerson, 2012; Merbs, Resnikoff, et al., 2015b).

To strengthen surgical training, the second edition of *Trichiasis Surgery for Trachoma* (Merbs, Resnikoff, et al., 2015a) provides a guide for training and certifying new trichiasis surgeons. Only surgeons who have been certified according to this protocol and assessed using the WHO manual *Final Assessment of Trichiasis Surgeons* (World Health Organization, 2005) should be allowed to conduct unsupervised practice. Further, supportive supervision, whereby a more experienced surgeon or surgical trainer regularly visits and observes less experienced surgeons operate and helps them to improve their technique and results, has been recommended as a way to improve surgical outcomes. Lastly, refresher training courses should be organized at national or regional level every 1–2 years and TT surgeons asked to attend (World Health Organization, 2016b). Such workshops would help to improve techniques and also to motivate staff.

According to the WHO GET2020 second Global scientific meeting on trachomatous trichiasis report, management of post-operative trichiasis is technically difficult, and is likely to be handled better by health-care workers with more specific formal technical training and/or greater professional experience (World Health Organization, 2016a). As such, GET2020 recommends that post-operative trichiasis should be managed by the most experienced trichiasis surgeon or eye specialist available. However, this recommendation should not restrict countries from setting their own standards defining who should manage post-operative trichiasis. In addition, programmes are encouraged to develop their own locally appropriate targets for good surgical outcomes, national policies and guidelines for monitoring outcomes and conducting surgical audits, and strategies for managing poor outcomes in pursuit of GET2020.

For countries that do not have a written national policy for the timing of follow-up and outcome assessment after trichiasis surgery, the ICTC preferred practice guidelines are recommended (International Coalition for Trachoma Control, 2015). These guidelines provide a framework for how to conduct an effective and efficient trichiasis surgical outreach program – from mobilizing patients to planning and organizing the outreach, surgical counselling, post-operative care, and recording and reporting program outputs. Several other guidelines, manuals and toolkits are also available to guide national trachoma programmes on how to monitor outcomes and conduct surgical audits and support their efforts in eliminating trachoma (Courtright & MacArthur, 2015; International Coalition for Trachoma Control, 2016).

In practice, however, monitoring of outcomes and auditing of surgeons' performance is infrequently done, especially in African settings. Most trachoma programmes lack effective routine systems and structures, policies and strategies for monitoring outcomes and conducting surgical audits. As such, patients are often lost to follow up after only a week which makes providing post-operative care and monitoring of outcomes difficult (International Coalition for Trachoma Control, 2015). To address this, community follow up of surgical cases should be routinely done on at least a selection of patients

PART B: LITERATURE REVIEW

of all surgeons, to determine if any retraining is needed. This can be incorporated into community trachoma screening and monitoring programmes.

Our study sought to assess the current national targets for good surgical outcomes, national policies and strategies for monitoring outcomes and conducting surgical audits, and strategies for addressing poor surgical quality among surgeons through a survey administered to trachoma programme managers in 29 trachoma-endemic countries in Africa.

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PART C: MANUSCRIPT

Manuscript 1

Post-operative trachomatous trichiasis in Africa: Systematic review

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ABSTRACT

Background

High incidence of post-operative trichiasis and other poor outcomes after surgery in most trachoma-endemic settings poses a major challenge to global elimination of trachoma. This systematic review aimed to assess the incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa, based on findings of observational and interventional studies.

Search methods

We searched PubMed, Academic Search Premier, Africa-Wide Information, CINAHL and Health Source Nursing through EBSCOhost, Web of Science [all databases], and Cochrane Central Register of Controlled Trials for relevant studies on the subject. We also searched the reference lists of included studies to identify further potentially relevant studies. We included all observational and interventional studies that measured post-operative trichiasis as one of the primary outcomes. Only studies conducted in Africa were included in this review.

Data collection and analysis

Two reviewers independently screened the titles and abstracts, selected and assessed the articles for inclusion in this review. Any disagreements were resolved through discussion or by consulting a third reviewer. Where necessary, the corresponding authors of included studies were contacted to provide any missing data. Our primary outcome was post-operative trichiasis, which was defined as any eyelash touching the globe at different time points after surgery.

Main results

Thirty-five studies, including 12,943 participants, met the inclusion criteria. A number of the studies included in this review utilized the same data to measure the incidence of post-operative trichiasis and other poor outcomes over different follow-up periods.

Overall, a review of the included studies revealed a pattern of high incidence of post-operative trichiasis and other poor outcomes ranging from 2.3 at 6 weeks to 65% at 7 years. This incidence varied by type of study design, surgical procedure and technique used as well as the follow up period among other factors.

Keywords: post-operative trichiasis, trachoma, trichiasis surgery

INTRODUCTION

Trachoma is the leading infectious cause of blindness worldwide. It is caused by particular strains of the intracellular bacterium *Chlamydia trachomatis* which is mainly transmitted through personal contact with infected persons as well as by flies that have been in contact with discharge from the eyes or nose of an infected person (World Health Organization, 2017). In the early stages of infection, trachoma is often subclinical. However, repeated infection leads to scarring of the tarsal conjunctiva, which, can then lead to trichiasis (eyelashes touching the globe), an advanced stage of trachoma. Left untreated, trachomatous trichiasis can result in the formation of corneal opacities which may lead to irreversible blindness (Taylor et al., 2014).

Surgery is an integral part of the World Health Organization SAFE strategy for elimination of trachoma as a public health problem (World Health Organization, 2015). It is recommended as treatment for trachomatous trichiasis to prevent trachoma-related blindness. Apart from correction of in-turned eyelids to preserve vision, surgery has also been shown to enhance patient comfort due to a decrease in photophobia and resolution of corneal swelling (Woreta et al., 2009). However, for surgery to be effective in preventing trachoma-related blindness, it must yield good long-term surgical outcomes with low incidence of post-operative trichiasis. According to recommendations of the third WHO global scientific meeting on trachoma (World Health Organization, 2010), national trachoma programmes should report the incidence of post-operative trichiasis, with a target of 10% or less incidence of post-operative trichiasis at one-year post-surgery. It has been previously noted that most studies conducted in trachoma-endemic countries have reported higher incidence of post-operative trichiasis and other poor outcomes following surgery, regardless of the surgical technique used (Burton et al., 2015).

Existing literature and data on post-operative trichiasis are highly inconsistent due to differences in study design, type of surgical technique used and varying follow up periods (West, Mkocha, Munoz, Mabey, Foster, Foster, et al., 2005). According to a Cochrane review of interventions for trachoma trichiasis (Burton et al., 2015), the average incidence of post-operative trichiasis reported in clinical trials is typically around 20% by one year after surgery. However, observational studies on post-operative trichiasis have reported higher figures ranging from 10% at 3 months to over 60% at 3 years (Reacher et al., 1990, 1992; Shannath, West & West, 2005; West, Mkocha, Munoz, Mabey, Foster, Bailey, et al., 2005a; Rajak, Collin & Burton, 2012; Habtamu et al., 2016). In addition, only limited operational data have been published from settings in which trachoma elimination programmes are active (Burton et al., 2015). Therefore, it is possible that under programmatic conditions, the cumulative incidence of post-operative trichiasis is even higher. Without a proper understanding of the magnitude and determinants of post-operative trichiasis in the region, it is difficult to have

informed discussions on the feasibility of the current target, develop strategies to improve surgery outcomes for trichiasis, or even to determine how urgent their development might be.

This review aims to fill this gap by consolidating data from various published and unpublished studies on outcomes of trichiasis surgery with a focus on incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa. The evidence will be useful in the planning and implementation of public health interventions to address post-operative trichiasis.

MATERIALS AND METHODS

Search Strategy

A comprehensive search was conducted to identify studies that have examined the incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa. The following electronic databases were searched: PubMed, Academic Search Premier, Africa-Wide Information, CINAHL and Health Source Nursing through EBSCOhost, Web of Science [all databases], and Cochrane Central Register of Controlled Trials.

In addition, Google Scholar® and other relevant websites were searched for grey materials. Reference lists of relevant reviews and all eligible papers were also hand-searched to identify relevant studies. The search strategy for electronic databases incorporated both Medical Subject Headings (MeSH terms) and free-text key terms which will be adapted to suit each individual database using applicable controlled vocabulary.

The following MeSH terms and key terms were used: ("Trichiasis"[Mesh] OR ("trichiasis"[MeSH Terms] OR "trichiasis"[All Fields])) OR ("Entropion"[Mesh] OR ("entropion"[MeSH Terms] OR "entropion"[All Fields])). The last search of the electronic databases was on 9 May 2018.

Study selection and characteristics

Two reviewers (GM, PC) independently screened the titles and abstracts of the articles found in the original search to determine their eligibility for inclusion. Thereafter, the full texts of potentially eligible studies were obtained, and the final selection for inclusion into the review conducted by the two reviewers. Any disagreements regarding inclusion of studies were resolved by discussion or by consulting a third reviewer (AS).

We included studies that met the following criteria: 1) conducted within Africa ; 2) measures post-operative trichiasis (defined as the presence of one or more eye lashes touching the globe or evidence of epilation after surgery) as one of the outcomes 3) the study participants were [a] for interventional studies: adults with un-operated trachomatous trichiasis or trachoma-related entropion of the upper lid in at least one eye or [b] for observational studies: adults with the presence of trachomatous trichiasis identified at the time of survey.

All relevant interventional and observational studies were included. Editorial articles, reviews, expert opinions and conference papers were excluded from the review as well as studies conducted outside Africa and those that did not measure post-operative trichiasis as one of the outcomes. There were no language and date restrictions during the search. However, in the end, we excluded studies conducted before 1990 as they were found not to be relevant to the review question.

Data extraction

Data from the included studies were extracted independently by two reviewers (GM, PC) using a standardised Joanna Briggs Institute data extraction form. The core information extracted included: study characteristics (title, author and year of publication), study design, number of participants and subject characteristics, surgery procedure(s) used, intervention group, control group and type of intervention (for comparative randomized controlled studies), follow up period and rate, incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery, as well as the associated risks if reported. Any discrepancies in data extraction were resolved by consensus between the two reviewers. Prior to use, the extraction form was piloted on at least four studies identified randomly from the list of included studies and modified accordingly. We did not find any missing data in the included studies.

Data Synthesis

Data from all included studies were compiled in an MS Excel spreadsheet and synthesised into two different tables in line with the two objectives of the review: to estimate the incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa and to compare the incidence of post-operative trichiasis and other poor outcomes in interventional studies and observational studies in Africa. Where possible, similar studies were grouped together to compare, broadly, similar types of outcome to produce overall estimates of effect, mostly based on the follow-up period. Due to the heterogeneity of study designs, follow-up periods and outcome reporting, a meta-analysis was not performed.

RESULTS

Flow of studies

Our initial electronic literature search yielded 5003 articles. After removal of duplicates and a review of titles and abstracts of these and other articles identified by hand searching, 97 full publications were selected for possible inclusion. Out of these, 61 articles were excluded due to the following reasons: conducted outside Africa ($n=23$), did not measure the outcome of interest (post-operative trichiasis) ($n=21$), the condition of interest was not trachomatous trichiasis ($n=3$), and finally, reviews, editorial articles and expert opinions ($n=14$). One prospective study conducted in Tunisia was subsequently also excluded from the review, despite having met the inclusion criteria, due to internal

inconsistencies in the study methods and reported findings. Figure 1 and Table 1 summarise the flow of literature search for this review and the list of excluded studies respectively.

Figure 1. Flow chart of the literature search

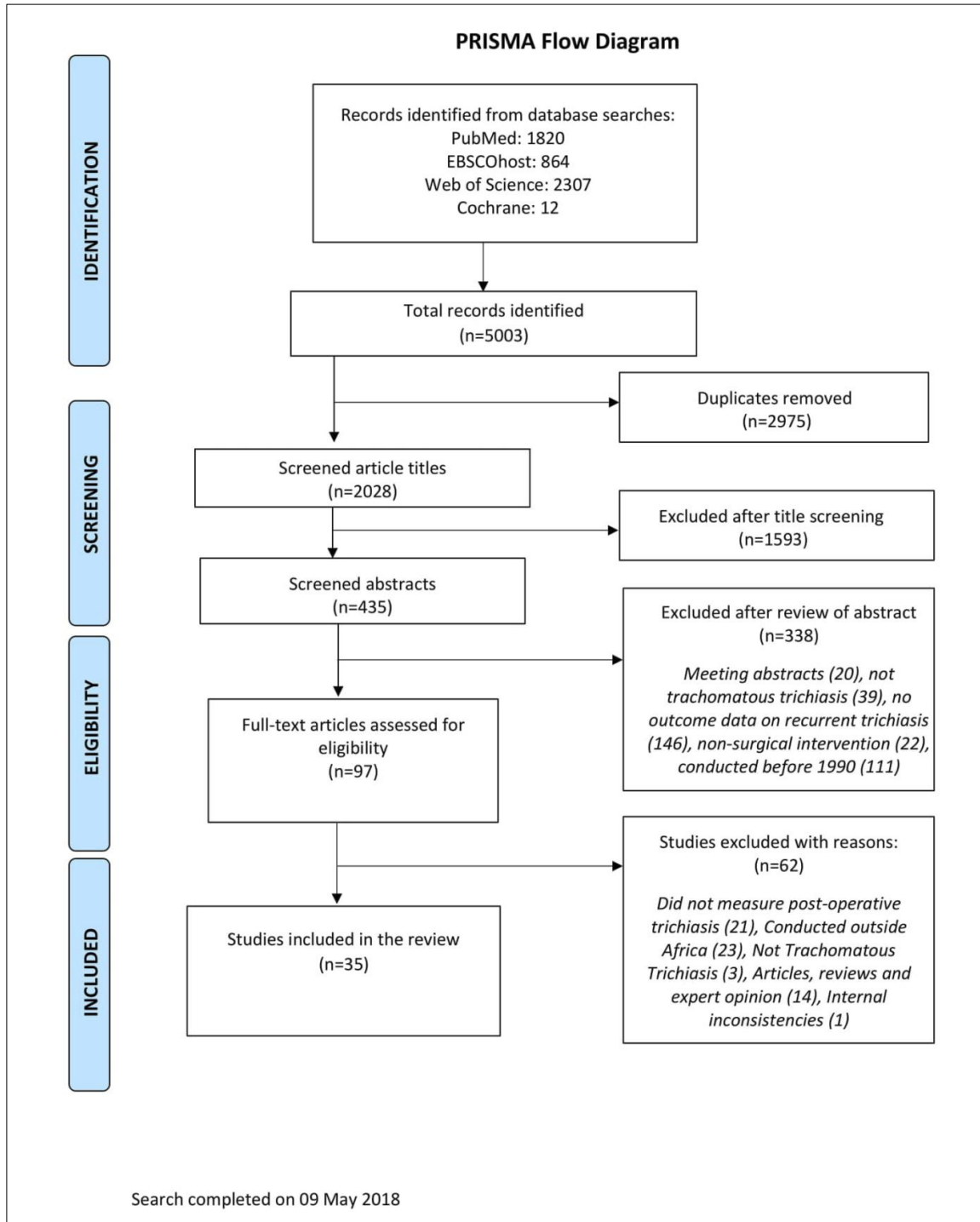


Table 1. Studies that were excluded from the systematic review

Author(s)	Year	Reason for exclusion
Conducted outside Africa		
Reacher <i>et al.</i>	1990	Conducted in Oman
Cruz <i>et al.</i>	1991	Conducted in Brazil
Reacher <i>et al.</i>	1992	Conducted in Oman
Stades <i>et al.</i>	1993	Conducted in Netherlands
Yeung <i>et al.</i>	1997	Conducted in Hong Kong
Beigi b	2001	Conducted in UK
Bujger <i>et al.</i>	2004	Conducted in Croatia
Dhaliwal <i>et al.</i>	2004	Conducted in India
Zhang <i>et al.</i>	2004	Conducted in Nepal
Sadiq & pai	2005	Conducted in Oman
Khandekar <i>et al.</i>	2006	Conducted in Oman
Moosavi <i>et al.</i>	2007	Country unspecified
Monga <i>et al.</i>	2008	Conducted in India
Bleyen & dolman	2009	Conducted in Canada
Sakarya <i>et al.</i>	2010	Conducted in Turkey
Ali <i>et al.</i>	2012	Conducted in Pakistan
Nakauchi <i>et al.</i>	2012	Conducted in Japan
Yagci & palama	2012	Conducted in Turkey
Barr <i>et al.</i>	2014	Conducted in Australia
Cruz <i>et al.</i>	2015	Conducted in Saudi Arabia
Ferraz <i>et al.</i>	2017	Conducted in Brazil
Russell & seiff	2017	Conducted in USA
Sendul <i>et al.</i>	2018	Conducted in Turkey
Different outcome		
Schémann <i>et al.</i>	1997	Prevalence of trachoma in the region
Bowman <i>et al.</i>	2001	Incidence of trichiasis
Ezz <i>et al.</i>	2001	Prevalence of trachoma
Frick <i>et al.</i>	2001	Cost of illness of untreated trichiasis
Bowman <i>et al.</i>	2002	Progression of trichiasis and corneal scarring
Wolle <i>et al.</i>	2010	Physical functioning of trichiasis surgery patients
Rajak <i>et al.</i>	2011	Corneal opacity
Gower <i>et al.</i>	2012	New grading scheme for eyelid contour abnormality
Merbs <i>et al.</i>	2012	Description of the new of TT clamp for trichiasis surgery
Merbs <i>et al.</i>	2012	Immediate post-operative eyelid contour
Li <i>et al.</i>	2013	Anti-scarring properties of doxycycline
Schein <i>et al.</i>	2016	Corneal sensitivity
Bickley <i>et al.</i>	2017	Uptake of surgery
Habtamu <i>et al.</i>	2015	Economic poverty
Habtamu <i>et al.</i>	2015	Vision and health related quality of life

Mousa <i>et al.</i>	2015	Uptake of trichiasis surgery
Oktavec <i>et al.</i>	2015	Perceptions of surgery 24 months
Smith <i>et al.</i>	2015	Prevalence of TT and CO
Thompson <i>et al.</i>	2015	Health beliefs and perceptions
Burr <i>et al.</i>	2016	Prevalence of TF and TT
Habtamu <i>et al.</i>	2016	Impact of trichiasis surgery on vision
Reviews & editorial articles		
Reacher & Taylor	1990	Review
Elder & Collins	1997	Editorial article
Bowman <i>et al.</i>	1999	Editorial article
Ruban & Baggio	2003	Article
Burton & Solomon	2004	Article
Yorston <i>et al.</i>	2006	Systematic review
Lin & Lietman	2007	Editorial
Kirkwood <i>et al.</i>	2011	Article
Rajak <i>et al.</i>	2012	Major review
Lockwood & Stern	2014	Systematic review
Burton <i>et al.</i>	2015	Systematic review
Habtamu & Burton	2015	Article
Ramadhani <i>et al.</i>	2016	Review
Solomon <i>et al.</i> , 2016	2016	Comment
Not trachomatous trichiasis		
Scheepers <i>et al.</i>	2010	Involitional lower eyelid entropion
Cevallos <i>et al.</i>	2012	Conjunctival bacterial infection
Burn <i>et al.</i>	2017	Podoconiosis
Other reasons		
Zbiba <i>et al.</i>	1993	Internal inconsistencies

Characteristics of included studies

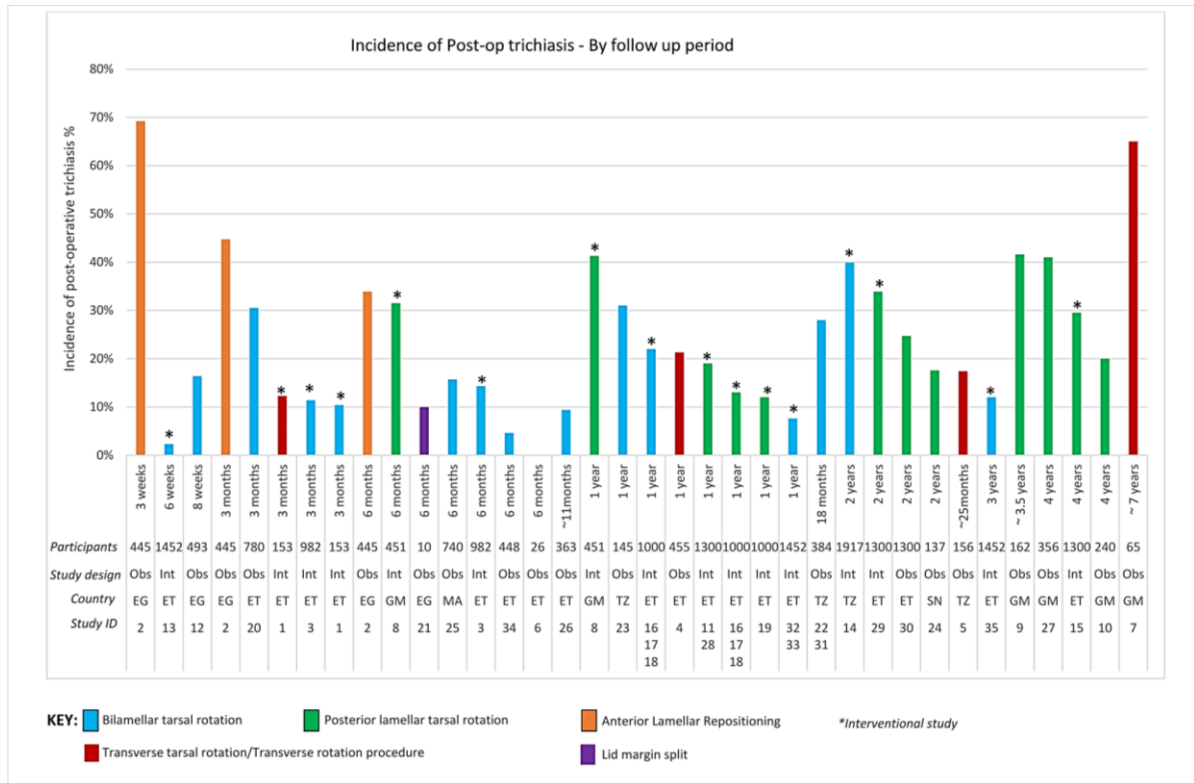
Thirty-five studies – 15 interventional and 20 observational studies - met the inclusion criteria with 12,943 participants – Appendix 1 and 2. A number of studies included in this review utilized the same data, or a subset of the same dataset, to measure the incidence of post-operative trichiasis over different follow up periods. For the purpose of this review, studies that used the same dataset were reported together to avoid duplication of results [example - (West *et al.*, 2006, 2007; Gower *et al.*, 2011; Woreta *et al.*, 2012)], while those that used a subset of the same dataset or had the same group of participants but different study designs were reported as separate studies.

Incidence of post-operative trichiasis and other poor outcomes of trichiasis surgery in Africa

From the 35 primary studies included in this review, the incidence of post-operative trichiasis varied widely from 2.3% at 6 weeks (Gower *et al.*, 2011) to 65% at 7 years (Bowman *et al.*, 2000). The follow up period also differed broadly from 3 weeks to several years. In terms of the surgical techniques, BLTR and PLTR were the most commonly reported procedures in included studies – in

16 and 13 studies respectively. Other surgical treatments featured in this review include Anterior Lamellar Rotation, Transverse tarsotomy and lid margin rotation and lid margin split (Adamu & Alemayehu, 2002; Ahmed & Abdelbaky, 2015; Bouazza et al., 2017). A majority of the studies included in this review were conducted in Ethiopia. Figure 2 below illustrates the cumulative incidence of post-operative trichiasis by follow up period as reported in the 35 studies in this review.

Figure 2. Incidence of post-operative trichiasis in Africa



Follow up period ≤ 6 months

In our review, we found a number of studies that had investigated the occurrence of post-operative trichiasis at 3 weeks, 6 weeks, 8 to 10 weeks, 3 months and 6 months. Among these, a study by (Ahmed & Abdelbaky, 2015) reported a high incidence of 69.2% lids presenting with post-operative trichiasis (one or more eyelashes) at 3-weeks after surgery. However, only 2.7% lids were considered as failure (≥ 6 lashes touching the globe) requiring repeat surgery; the rest did not require further surgical intervention although they needed more than two sessions of electrolysis or laser ablation. Similar results were reported in another study conducted in Ethiopia (Gower et al., 2011) where 2.3% of the operated eyelids developed post-operative trichiasis, 1.2% had eyelid contour abnormalities, 10.5% had granuloma formation and 1.3% had an eyelid closure defect at 6 weeks after BLTR surgery.

In contrast, a previous study conducted in Egypt reported a much higher incidence of post-operative trichiasis (16.4%) at 8 weeks after BLTR surgery (el Toukhy, Lewallen & Courtright, 2006). In this

study, the use of silk sutures was identified as the most significant risk factor for poor outcomes. Other risk factors associated with post-operative trichiasis and other poor outcomes in the weeks after surgery include surgeon's experience and technique, short incisions, baseline severity of the disease and epilation before surgery (el Toukhy, Lewallen & Courtright, 2006; Gower et al., 2011).

At 3 months post-surgery, we identified 4 studies which reported variable incidence of post-operative trichiasis ranging from 11.4% to 44.7% (Adamu & Alemayehu, 2002; Alemayehu et al., 2004; Kerie & Bejiga, 2010; Ahmed & Abdelbaky, 2015) – Table 2. A number of other poor outcomes were also reported to have occurred within this follow up period among them; overcorrection, lid notching, pyogenic granuloma, local madarosis and conjunctival and eyelid inflammation. An interventional study that compared the success rates of BLTR and Transverse Tarsotomy and lid margin Rotation (TTR) at the 3-month follow up mark found that, there were more cases of post-operative trichiasis in the TTR group compared to the BLTR although the latter had higher incidences of other poor outcomes and complications such as over correction, lid notching and granuloma (Adamu & Alemayehu, 2002).

Table 2. Studies with a 3-month follow up period

Study author, year	Country	Study Design	Follow up period	Results	
				Post-operative trichiasis	Other poor outcomes
(Adamu & Alemayehu, 2002)	Ethiopia	RCT	3 months	11.4% in both treatment groups. (10.4% BLTR; 12.3% TTR)	Overcorrection, lid notching, pyogenic granuloma
(Alemayehu et al., 2004)	Ethiopia	RCT	3 months	11.4% patients developed post-operative trichiasis within 3 months.	None reported
(Ahmed & Abdelbaky, 2015)	Egypt	Prospective non-comparative study	3 months	336/752 (44.7%) eyelids suffered post-operative trichiasis; 11.3% lids had ≥ 6 lashes	None reported
(Kerie & Bejiga, 2010)	Ethiopia	Design: Cross sectional survey	3 months	238/780 (30.5%) by person; 308/1317 (23.4%) by eyelids.	Conjunctival and eye lid inflammation – 32.4%

At 6 months, a prospective non-comparative study conducted in Egypt (Ahmed & Abdelbaky, 2015) reported a 33.9% incidence of post-operative trichiasis after ALR procedure. This was comparable to 31.5% reported in a randomized controlled trial conducted in The Gambia (Burton, Kinteh, et al.,

2005). This high incidence of post-operative trichiasis occurring in the first 6 months of surgery has been significantly associated with severity of the preoperative disease and the surgeons' skills.

Other studies with 6 months follow up period reported average incidence of post-operative trichiasis – 10% (Khafagy, Mostafa & Fooshan, 2012); 14.3% (Alemayehu et al., 2004) and 15.7% (Négre et al., 2000). In contrast, a study conducted in Ethiopia, using data from the STAR trial, reported relatively low incidence of post-operative trichiasis - only 36 of the 790 (4.6%) eyes that had surgery developed post-operative trichiasis at 6 months (Woreta et al., 2009).

Another study which was aimed at assessing the functional and aesthetic results of anterior lamellar resection with lid margin splitting of the upper lid in the treatment of cicatricial trachomatous entropion in Ethiopia reported no cases of post-operative trichiasis over the 6-month follow up period (Bouazza et al., 2017). In this case, anterior lamellar resection with lid margin splitting of the upper eyelid was found to be an effective technique in reducing the risk of post-operative trichiasis as well as significantly enhancing the aesthetic results of surgery for cicatricial trachomatous entropion.

Table 3. Studies with a follow up period of 6 months and above (<1 year)

Study author, year	Country	Study Design	Follow up period	Results	
				Post-operative trichiasis	Other poor outcomes
(Burton, Kinteh, et al., 2005)	The Gambia	RCT	6 months	129/410 (31.5%)	
(Alemayehu et al., 2004)	Ethiopia	RCT	6 months	140 (9%) eyelids of 124 (14.3%) patients	None
(Ahmed & Abdelbaky, 2015)	Egypt	Prospective non-comparative study	6 months	255/752 eyelids (33.9%) suffered post-operative trichiasis; of these 112 (14.9%) had ≥ 6 lashes	Local madarosis developed in 5.72% of the operated eyelids by the end of the follow up period
(Négre et al., 2000)	Morocco	Cross-sectional survey	> 6 months	117 of 740 people (15.8%)	Overcorrection: 2.3%; Ptosis: 0.4%; Lid necrosis without corneal exposure: 3.6% Lid necrosis with corneal exposure: 0.14%; Granuloma: 0.95%
(Khafagy, Mostafa & Fooshan, 2012)	Egypt	Prospective study	6 months	2/20(10%) eyelids of 2 patients developed post-operative trichiasis	Mild lid edema occurred in all patients postoperatively, which resolved within 1 week.

(Pearson et al., 2013)	Ethiopia	Cross-sectional survey	~11 months	34/363 (9.4%) patients	Granulomata 0.6%; lid closure defects 5.5% and lid notching 16.8%.
(Woreta et al., 2009)	Ethiopia	Prospective study within the STAR trial	6 months	36/790 (4.6%) operated eyelids developed post-operative trichiasis	Pain – 1.4% Photophobia – 0.9%
(Bouazza et al., 2017)	Ethiopia	Descriptive cross-sectional study	6 months	During the follow-up period, no cases of post-operative entropion were reported.	In 3 patients, a residual contact of one or a few eyelashes (<5 eyelashes) persisted.

Follow up period of 1 year

Most of the studies included in this review had a follow up period of 1 year and above. 11 studies; 8 interventional and 3 observational studies had a follow up period of one year – Table 4. The one-year incidence of post-operative trichiasis reported in these studies was between 7.6% and 41.3% (Burton, Kinteh, et al., 2005; West et al., 2006, 2007; Assefa et al., 2008; Rajak et al., 2011a; Burton et al., 2012; Merbs et al., 2015; Habtamu et al., 2016, 2017a,b, 2018). The highest incidence of post-operative trichiasis in this group (41.3%) was reported in an RCT conducted in the Gambia to investigate whether enhance control of infection using azithromycin could improve surgical outcomes in a trachoma control programme (Burton, Kinteh, et al., 2005). In this study, there was no significant difference in the incidence reported in the azithromycin group (41.2%) and the control (tetracycline) group (41.4%) meaning that azithromycin did not have a protective effect against post-operative trichiasis contrary to what was reported in (West et al., 2006, 2007).

Table 4. Studies with 1-year follow up period

Study author, year	Country	Study design	Follow up period	Results	
				Post-operative trichiasis	Other poor outcomes
(Burton, Kinteh, et al., 2005)	The Gambia	RCT	1 year	Overall, 176/426 (41.3%)	27 cases of corneal opacification
(Burton et al., 2012) (Rajak et al., 2011a)	Ethiopia	RCT	1 year	234/1236 (19%) participants	Granulomata – Absorbable suture group (5.7%), silk suture group (8.7%) Notching – 14% in absorbable suture group and 11.9% in the silk suture group
(Habtamu et al., 2016, 2017b,a)	Ethiopia	RCT	1 year	Cumulative incidence at 12 months: 173/992 (17.4%) patients	Granulomata: PLTR – 5.2%, BLTR – 2.2% ECAs – PLTR – 6.3%, BLTR – 7.6%

(West et al., 2006)	Ethiopia	RCT	1 year	Cumulative incidence – 107/1414 (7.6%)	1.3% eyelid closure defect; 1.2% eyelid contour abnormalities 10.5% pyogenic granuloma formation
(West et al., 2007)					
(Merbs et al., 2015)	Tanzania	Preliminary data analysis from the PRET trial	1 year	77/245 (31%) eyelids had postoperative trichiasis	None reported
(Assefa et al., 2008)	Ethiopia	Prospective study	1 year	93 of the 560 (16.6%) operated lids upper eyelids. In terms of persons, 77 (21.3%) of the 361 patients	None reported
(Habtamu et al., 2018)	Ethiopia	RCT	1 year	120/999 (12%) patients developed post-operative trichiasis;	None reported

Other poor outcomes reported at one-year follow up included chlamydial infection, granulomas, eyelid closure defect, ECAs and lid notching. Some of the risk factors associated with post-operative trichiasis at one-year include severe preoperative trichiasis, bacterial infection and severe baseline conjunctival inflammation (Burton, Kinteh, et al., 2005) as well as surgeon-related factors such as inadequate peripheral dissection, irregular incision, asymmetric suture position and tension, inadequate correction, and lash location (Habtamu et al., 2016, 2017b).

Follow up > 1 year

The maximum follow-up period reported in the studies included in this review was a median time of 7 years after surgery – range not specified (Bowman et al., 2000). In this study which was conducted in the Gambia, a cumulative incidence rate of 65% or 55% in terms of the number of operated eyelids that suffered post-operative trichiasis was reported (Bowman et al., 2000). High incidence rates over different follow up periods above one year were also reported in a number of other studies; 41.6% over an average follow up period of 3.5 years (Burton, Bowman, et al., 2005), 41% over a 4-year follow up period (Rajak et al., 2010), 39.9% and 33.9% over a 2-year follow up period in (Gower et al., 2013) and (Habtamu et al., 2015) respectively.

This high incidence of post-operative trichiasis over long-term follow up period was attributed to accumulation of early cases of post-operative trichiasis, differences in surgical technique (Habtamu et al., 2017b), bacterial infection, tarsal conjunctival inflammation and post-operative environment (West, Mkocho, Munoz, Mabey, Foster, Bailey, et al., 2005b). One study conducted by in a trachoma-endemic area of central Tanzania concluded that, occurrence of post-operative trichiasis 18

months after surgery was associated with the technique, skill, and experience of the surgeon (West, Mkocha, Munoz, Mabey, Foster, Bailey, et al., 2005a).

Other poor outcomes reported over long-term follow up period include granulomata (16.8%) and ECAs (16.3%) reported in (Gower et al., 2013) following BLTR surgery with either a TT clamp or the standard BLTR equipment within 2-year follow up period. Similar outcomes of granulomata, lid notching and cases of visually significant corneal opacity were also reported in other studies at 2 and 4 years after surgery (Rajak et al., 2010, 2013).

Table 5. Studies with over 1 year follow up period

Study author, year	Country	Study Design	Follow up period	Results	
				Post-operative trichiasis	Other poor outcomes
(Gower et al., 2013)	Tanzania	RCT	2 years	Overall incidence – 1333/3343 (39.9%) eyelids	Granulomata - TT clamp (16.8%), standard BLTR group (22.4%) ECAs - TT clamp Group (16.3%), standard BLTR group (23.7%)
(Habtamu et al., 2015) (Rajak et al., 2011b)	Ethiopia	RCT	2 years and 4 years	<u>At 2 years</u> 412/1216 (33.9%) patients; <u>At 4 years:</u> 340/1151 (29.5%)	Lid margin conjunctivalisation was higher in the epilation-only group
(Woreta et al., 2012)	Ethiopia	RCT	3 years	<u>At 3 years:</u> 10% in the azithromycin group; 13% in the topical tetracycline group	None reported
(Bowman et al., 2000)	The Gambia	Retrospective Cross-sectional study	Median time since surgery was 7 years	63/115 (55%) operated eyes in 42/65 (65%) people had suffered post-operative trichiasis.	4 of 115 operated eyes (3.5%) had inadequate lid closure and corneal exposure. 3 of these had central corneal opacity.
(Burton, Bowman, et al., 2005)	The Gambia	Retrospective cohort study	Mean: 3.5 years (range: 2.9–4.5 years)	At follow up 89/214 (41.6%) previously operated eyes had suffered post-operative trichiasis	General deterioration in visual acuity between surgery and follow up, which was greater if new corneal opacification developed or trichiasis returned.
(Rajak et al., 2010)	The Gambia	Prospective study	4 years	Incidence of post-operative trichiasis at 4 years: 41%	At 4 years, 98 (36%) study eyes had visually significant Corneal opacity.

(Merbs, West & West, 2005) (West et al., 2005b)	Tanzania	Retrospective cohort	> 18 months	176/630 (28%) eyes developed post-operative trichiasis	None reported
(Rajak et al., 2013)	Ethiopia	Prospective	2 years	Overall, post-operative trichiasis occurred in 315/1276 (24.7%) study eyes within the 2 years	Within 2 years, Granuloma occurred in 69 (5.7%) and notching in 156 (13.0%).
(Burton et al., 2010)	The Gambia	Prospective cohort study	4 years after surgery	By 4 years, 24 (20%) of these 117 people had incident post-operative trichiasis.	None reported
(Ndoye et al., 1997)	Senegal	Retrospective study	2 years	Incidence of post-operative trichiasis over a 2-year study period: 17.6%	None reported
(Bog, Yorston & Foster, 1993)	Tanzania	Prospective community-based study	Mean 25.5 months (9-36 months)	Cumulative incidence at the last follow up was 17.4% .	1 eye developed a wound infection 9 eyes (6.3%) developed minimal central notching of the upper eyelid within the follow up period.

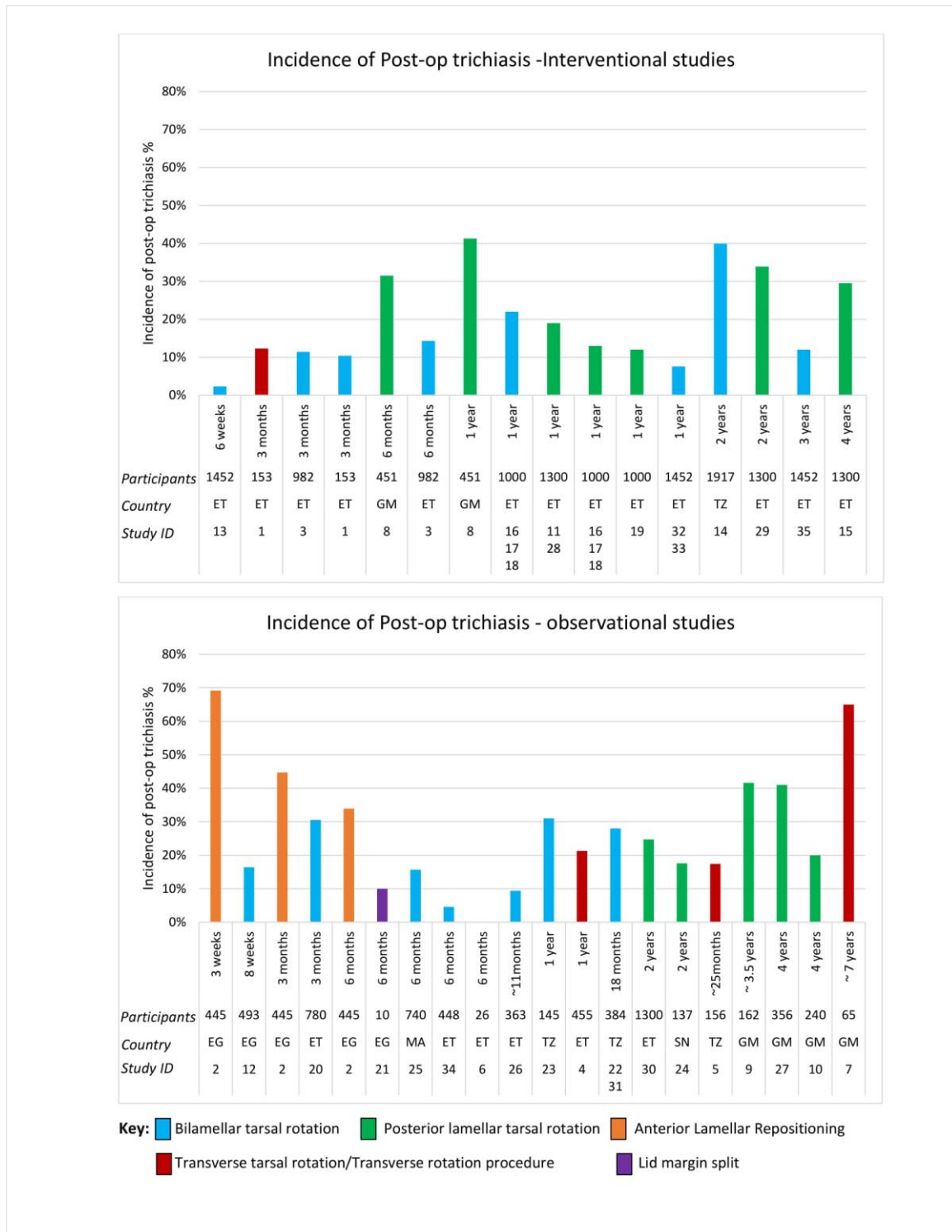
Comparison between interventional studies and observational studies in Africa

A comparison between the two broad types of studies revealed varying the incidence of post-operative trichiasis reported in both interventional and observational studies across different follow up periods and surgical techniques. However, generally, the reported incidence of post-operative trichiasis was lower in interventional studies (Burton, Kinteh, et al., 2005; Rajak et al., 2011a; Gower et al., 2013; Habtamu et al., 2015, 2016, 2017a,b) compared to the observational studies (Bowman et al., 2000; West, Mkocha, Munoz, Mabey, Foster, Bailey, et al., 2005b; Burton, Bowman, et al., 2005; Merbs, West & West, 2005; Assefa et al., 2008; Burton et al., 2010; Kerie & Bejiga, 2010; Rajak et al., 2010, 2013; Ahmed & Abdelbaky, 2015; Merbs et al., 2015) – see Figure 3 below.

Among the 16 interventional studies included in this review, the highest incidence of post-operative trichiasis reported was 41.3% at 1-year follow up reported in a randomised controlled trial conducted in the Gambia (Burton, Kinteh, et al., 2005) while the lowest incidence was 2.3% at 6 weeks post-operative follow up reported in a study conducted in Ethiopia (Gower et al., 2011). In both studies, the role of azithromycin in reducing the risk of post-operative trichiasis was investigated. Other interventions investigated in the interventional studies in this review include use of absorbable sutures (Rajak et al., 2011a), the use of a TT clamp to improve BLTR surgery outcomes (Gower et al., 2013),

the use of oral doxycycline to reduce the risk of post-operative trichiasis (Habtamu et al., 2018) and comparison between different surgical techniques (Adamu & Alemayehu, 2002; Rajak et al., 2011b; Habtamu et al., 2015, 2016) and outcomes of surgery done by ophthalmologists versus trained IECWs (Alemayehu et al., 2004).

Figure 3. Incidence of post-operative trichiasis - interventional vs observational studies



In observational studies, on the other hand, high incidence of post-operative trichiasis were reported at 3 weeks (69.2%) (Ahmed & Abdelbaky, 2015) and 65% in another study with a median follow up period of 7 years (Bowman et al., 2000). At the recommended 3-6 months follow up, two interventional studies (Adamu & Alemayehu, 2002; Alemayehu, 2004) reported comparable incidence of post-operative incidence at 3 months; 11.4% (Alemayehu et al., 2004) and 10.4% in BLTR group, 12.3% in TTR group (Adamu & Alemayehu, 2002). These were significantly lower than the incidence rates reported in the two observational studies; 44.7% (Kerie & Bejiga, 2010) and 30.5% (Ahmed & Abdelbaky, 2015) over the same follow up period. In addition, there were more poor outcomes reported in the observational studies compared to the interventional studies at 3 months post-surgery. At 6 months, the incidence of post-operative trichiasis reported in one interventional study – 31.5% (Burton, Kinteh, et al., 2005) was higher than the incidence reported in other interventional studies (Alemayehu et al., 2004) but comparable to the figures reported in various observational studies (33.9% (Ahmed & Abdelbaky, 2015), 32% (Rajak et al., 2010) over the same period.

At one-year follow up, lower incidence rates (7.6% to 19%) were reported in interventional studies compared to the observational studies (9.4% to 40%), with the exception of one clinical trial conducted in the Gambia (Burton, Kinteh, et al., 2005) which reported a 41.3% incidence of post-operative trichiasis at the one year follow up. In this randomised controlled trial, the one-year incidence of post-operative trichiasis in the two study arms were almost similar with 41.2% in the Azithromycin arm and 41.4% incidence in the control arm, which implied that azithromycin did not improve outcomes of PLTR surgery. This rate was higher than the one-year incidence figures reported in other interventional studies (West et al., 2007; Habtamu et al., 2016), but comparable to those reported in some observational studies (Rajak et al., 2010; Merbs et al., 2015).

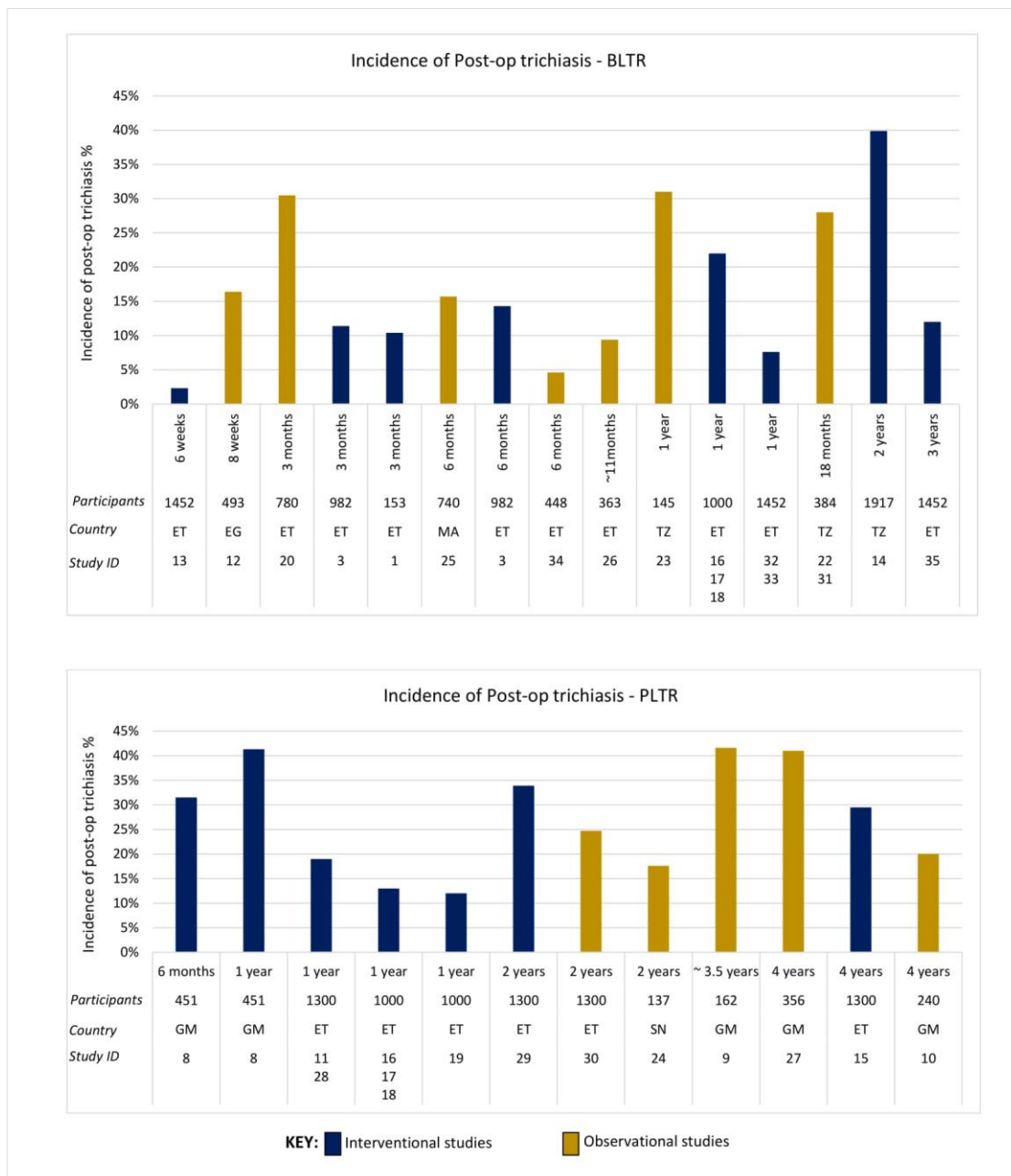
Comparison between surgical procedures and techniques

In terms of the surgical procedure, the two procedures recommended by WHO - PLTR and BLTR were the most commonly used surgical techniques in the studies included in this review. Other procedures whose outcomes were measured and reported in the included studies include: anterior lamellar repositioning, transverse tarsal rotation with lid margin rotation and lid margin split combined with cryotherapy. Unfortunately, high incidences of post-operative trichiasis were reported across the different studies regardless of the procedure used – 69.2% at 3 weeks using ALR (Ahmed & Abdelbaky, 2015); 41.3% at 1 year using PLTR (Burton, Kinteh, et al., 2005); 39.9% at 2 years using BLTR (Gower et al., 2013); and 65% at 7 years using tarsal rotation procedure (Bowman et al., 2000).

Overall, however, PLTR was found to yield better outcomes compared to repeated epilation [PLTR (17.5%), epilation (49.4%)] (Rajak et al., 2011b) and had lower incidence of post-operative trichiasis

compared to the BLTR (13% versus 22%) (Habtmu et al., 2016) – See Figure 5. On the other hand, BLTR was found to yield better outcomes compared to TTR for treatment of trichomatous trichiasis of the upper lid with reduced early incidence of post-operative trichiasis (10.4% in BLTR compared to 12.3% in the TTR group) at 3 months follow up, although this difference was not statistically significant (Adamu & Alemayehu, 2002). These variations in the incidence of post-operative trichiasis by surgical technique are attributable to fundamental differences in the surgical methods. In this case, PLTR has been found to achieve a more stable and long-lasting correction compared to BLTR and other (Habtmu et al., 2016).

Figure 4. Incidence of post-operative trichiasis - BLTR vs PLTR



In an interventional study conducted in Tanzania, high incidence of poor outcomes after BLTR surgery using either the TT clamp or standard BLTR procedure (60.9% vs 63.0%, respectively) were reported (Gower et al., 2013). Although the TT clamp was somewhat protective against lid contour abnormalities and granuloma formation, it did not reduce the incidence of post-operative trichiasis 2-years post-surgery (Gower et al., 2013). These results were comparable to the 2-year cumulative incidence of post-operative trichiasis (33.9%) reported in a surgery versus epilation non-inferiority trial conducted in Ethiopia (Rajak et al., 2011b) and a number of other observational studies (Burton, Bowman, et al., 2005; Rajak et al., 2010).

In observational studies, both BLTR and PLTR surgical techniques produced comparable outcomes, although these were higher than the figures in the interventional studies with similar interventions (Adamu & Alemayehu, 2002; el Toukhy, Lewallen & Courtright, 2006; Assefa et al., 2008; Merbs et al., 2015; Habtamu et al., 2016). Community based trichiasis surgery performed by a trained ophthalmic nurse was found to be as effective as surgery performed in a health centre (Bog, Yorston & Foster, 1993).

Regarding the surgical technique, lower incidence of post-operative trichiasis in cases with an incision height of ≥ 4 mm from the lid margin in BLTR surgery (Merbs et al., 2015). In this case, a longer incision is recommended as it allows the distal segment to rotate adequately, and once secured with sutures, it is less likely to revert to the original entropic position (Merbs, West & West, 2005; Merbs et al., 2015). However, there was no evidence that use of absorbable sutures was associated with a lower incidence of post-operative trichiasis at 1-year post surgery compared to the silk sutures, although absorbable sutures were found to reduce the incidence of granuloma (Rajak et al., 2011a; Burton et al., 2012).

Administration of a single dose of azithromycin was found to reduce the incidence of postoperative trichiasis by one third compared to the usual post-operative care using topical tetracycline, provided that the surgeons were properly trained and their skills standardized (West et al., 2006, 2007) but doxycycline did not reduce the risk of postoperative trichiasis and is therefore not indicated for the improvement of outcomes following trachomatous trichiasis surgery (Habtamu et al., 2018). There was no difference in risk of poor outcomes in surgeries performed by ophthalmologists versus those performed by the IECWs (Alemayehu et al., 2004; Assefa et al., 2008).

DISCUSSION

Evidence suggests that under operational conditions, there is a huge disparity in the incidence of post-operative trichiasis and other outcomes in Africa, and in most settings, these surgical outcomes are often poor. WHO recommends that all national trachoma elimination programmes should strive to achieve a 10% or less incidence of post-operative trichiasis at one year after surgery (World Health

Organization, 2010). However, based on the evidence presented in the studies included in this review, the incidence of post-operative trichiasis and other poor outcomes in programmatic settings may be much higher across different follow up periods (Bowman et al., 2000; Merbs, West & West, 2005; Burton, Bowman, et al., 2005; Burton, Kinteh, et al., 2005; Rajak et al., 2010, 2011b, 2013; Kerie & Bejiga, 2010; Gower et al., 2013; Ahmed & Abdelbaky, 2015; Merbs et al., 2015; Habtamu et al., 2015, 2016, 2017b,a).

Specifically, most observational studies in this review reported high incidences of post operative trichiasis (Bowman et al., 2000; West, Mkocho, Munoz, Mabey, Foster, Bailey, et al., 2005b; Burton, Bowman, et al., 2005; Merbs, West & West, 2005; Assefa et al., 2008; Burton et al., 2010; Kerie & Bejiga, 2010; Rajak et al., 2010, 2013; Ahmed & Abdelbaky, 2015; Merbs et al., 2015) while in interventional studies, and under strict surgical conditions, better outcomes with low incidence of post-operative trichiasis were reported in some settings (Adamu & Alemayehu, 2002; Alemayehu et al., 2004; West et al., 2006, 2007; Woreta et al., 2012). In a large randomized controlled trial conducted in a hyper endemic trachoma region in Ethiopia, a single dose of postsurgical azithromycin was significantly associated with a 33% reduction in incidence of post-operative trichiasis up to 3 years, compared with topical tetracycline prescribed for 6 weeks (West et al., 2006, 2007; Woreta et al., 2012). These results differ from a smaller clinical trial of azithromycin compared with 2 weeks of topical tetracycline conducted among patients with trichiasis in a hypo endemic trachoma region in The Gambia (Burton, Kinteh, et al., 2005). One important difference between these two trials was the absence of training and standardization of surgeons in the Gambia study, which might have resulted in high incidence of post-operative trichiasis (41.3%) at one year, with significant variability between surgeons ranging (0 to 83%).

In contrast, the Ethiopia STAR trial (West et al., 2006) used IECWs who had been trained and certified for surgery by the study team using the WHO guidelines to ensure quality, hence the better outcomes which were enhanced by the use of azithromycin. In this case, even though azithromycin may have a long-term protective effect against post-operative trichiasis, it cannot overcome the profound surgeon effects resulting from lack of adequate training, standardization and supervision of trichiasis surgeons. This is an indication that, under suitable circumstances, better outcomes can be achieved in Africa but in order to achieve this, policies and strategies are needed to redefine how training and supervision of trichiasis is done within the national trachoma programmes. With proper training and supervision of surgeons, the administration of azithromycin post-operatively can further reduce the incidence of post-operative trichiasis and other poor outcomes, especially in areas where trachoma is still active (West et al., 2006).

Another interpretation of the difference in the effect seen in these two trials was the presumed higher *C. trachomatis* transmission intensity in Ethiopia. This would tend to confer a higher likelihood of

peri-operative conjunctival *C. trachomatis* infections, which would be pro-inflammatory if not resolved by adjunctive treatment with azithromycin.

In a randomized controlled trial of the new TT clamp versus standard BLTR procedure, the two-year incidence of post-operative trichiasis was high in both arms of the study and although the new clamp appeared to offer protection against granuloma formation and some eyelid contour abnormalities, it did not reduce postoperative TT (Gower et al., 2013). This inconclusive results are possibly due to the sub-optimal training of trichiasis surgeons involved in the trial (only one training was held at the beginning of the trial) and the widely varying skill levels among several surgical technicians involved in the trial. In this case, the interval between training and the actual time when the technicians performed the surgeries varied across surgical technicians and may have affected outcomes. This once again highlights the importance of adequate training and standardization of surgeons' skills and procedures for better outcomes.

In (Rajak et al., 2011a), there was no evidence that use of absorbable sutures are associated with a lower incidence of post-operative trichiasis at 1-year post surgery compared to the silk sutures, although absorbable sutures were found to reduce the incidence of granuloma (Rajak et al., 2011a; Burton et al., 2012). In this trial, despite careful standardisation procedures, there was still some variation between the results of the different surgeons, indicating the importance of how the surgery is performed. Currently, BLTR and PLTR are the most common procedures and have been found to produce better outcomes compared to other procedures in the treatment of TT (Adamu & Alemayehu, 2002; Rajak et al., 2011b; Habtamu et al., 2015). However, in the past, there has been insufficient evidence comparing the two tarsal rotation procedures (BLTR and PLTR) to warrant preference of one procedure over the other until recently when a randomised controlled clinical trial conducted in Ethiopia found that, with ample training, practice and standardisation of surgeons, PLTR surgery was superior to BLTR surgery in terms of lower incidence of post-operative trichiasis and fewer intraoperative and immediate postoperative complications one-year after surgery (Habtamu et al., 2016). This means that PLTR could be the preferred procedure for the programmatic management of trachomatous trichiasis in Africa although more trials to compare the long-term outcomes of the two procedures - BLTR and PLTR are still needed.

It is important to note that, most the studies included in this review were conducted before adoption of the WHO training and certification manuals (World Health Organization, 2005, 2015) and ICTC training and certification guidelines (International Coalition for Trachoma Control, 2015). It is therefore likely that, with improved training [for example using HEAD START (International Coalition for Trachoma Control, 2018)] and improved supervision, the outcomes of trichiasis surgery are better. In this case, further research is needed to compare the incidence of post-operative trichiasis in patients operated on by surgeons trained with and without mannequins.

In conclusion, surgery for trichiasis is one of the core pillars of the WHO SAFE strategy for trachoma control. However, the current high and variable incidence of post-operative trichiasis and other poor outcomes after surgery poses a major challenge for national trachoma programmes as most patients who develop post-operative trichiasis are either lost during follow up or when found, many tend to refuse repeat surgery (Oktavec et al., 2015). In addition, the growing cases of post-operative trichiasis in trachoma-endemic countries add on to the already existing backlog of trichiasis cases, thereby increasing the trichiasis burden in these countries.

Results from interventional studies have demonstrated that, with proper interventions such as proper training/ retraining and certification of trichiasis surgeons, supportive supervision, standardisation procedures and administration of azithromycin post-operatively adequate training, better outcomes can be achieved. Therefore, there is need for national trachoma programmes to adopt and implement some of these interventions within programmatic settings in order to reduce post-operative trichiasis and other poor outcomes in Africa. However, even under strict surgical conditions, the one-year incidence of post-operative trichiasis is infrequently within the recommended 10% or less. For instance, in a randomised controlled trial comparing the outcomes of PLTR versus BLTR, the cumulative incidence of post-operative trichiasis at one-year was >10% in both groups, despite ample pre-trial training, practice, and assessment to bring the surgeons to a proficient standard (Habtamu et al., 2016). As such, there may be need for WHO to review the 10% recommendation in light of the existing evidence to reflect the real situation within programmatic settings.

Lastly, there is need for policies and strategies to standardize the follow-up period for trichiasis patients after surgery within national trachoma programmes. While WHO recommends a follow-up period of 3-6 months (World Health Organization, 2016), existing evidence in published studies has shown that the follow up period varies widely from a few weeks to several years. Moreover, cases of post-operative trichiasis continue to occur several years after surgery (Bowman et al., 2000; Burton, Bowman, et al., 2005; Burton et al., 2010; Rajak et al., 2010; Woreta et al., 2012; Habtamu et al., 2015). As such, strategies and systems to enhance patient follow-up and manage post-operative trichiasis cases within the national trachoma programmes beyond the recommended follow-up period should be considered.

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Supplementary Materials: List of included studies

Appendix 1: Interventional studies

Study ID	Study author, year	Country	Study characteristics	Follow up period	Results		Comments
					Post-operative trichiasis	Other poor outcomes	
1	(Adamu & Alemayehu, 2002)	Ethiopia	<p>Objective: To compare the success rates of two surgical methods: BLTR and TTR for trachomatous trichiasis of the upper lid.</p> <p>Design: RCT - Intervention group: BLTR - Control group: TTR Procedure/s: BLTR and TTR</p> <p>Number of participants/eyelids: 256 eyelids of 153 patients with TT; BLTR - 124 eyelids, TTR - 132 eyelids</p> <p>Primary outcome measure: Post-operative trichiasis defined as lash/eyeball contact in all position of gaze or inward rotation of the lid margin.</p>	3 months Follow up rate: 92.6% (237 eyelids of 141 patients) completed follow up; BLTR (115 eyelids), TTR (122 eyelids)	27 of 237 eyelids (11.4%) in both treatment groups. In the BLTR group, 12/115 eyelids (10.4%) had post-operative trichiasis. In the TTR group, 15/122 eyelids (12.3%) had post-operative trichiasis.	Overcorrection - 4/115 eyelids (3.5%) in the BLTR group but none in the TTR group.	Although the incidence of post-operative trichiasis was higher in the TTR group than in the BLTR group, complications such as lid-notching, pyogenic granuloma were more in the BLTR group than in the TTR group at 3 months follow up.
3	(Alemayehu et al., 2004)	Ethiopia	Objective: To study the outcome of Bilamellar tarsal rotation (BLTR) trichiasis surgery performed by ophthalmologists versus that done by integrated eye care workers (IECWs).	3 and 6 months Follow up rates:	<u>At 3 months</u> 11.4% of those examined, had post-operative trichiasis	None	The difference in the incidence of post-operative trichiasis observed in the group of patients operated on by ophthalmologists

			<p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: Surgery by an ophthalmologist - Control group: Surgery by an integrated eye care worker <p>Procedure/s: BLTR</p> <p>Number of participants/eyelids: 1750 eyelids of 982 patients with trichiasis</p> <p>Primary outcome measure: Post-operative trichiasis (one or more lashes touching any part of the globe in primary position following surgery).</p>	<p>At 3 months: 713/982 patients (73%)</p> <p>At 6 months: 694/901 patients (77%)</p>	<p><u>At 6 months,</u> Cumulative incidence of post-operative trichiasis was 140 (9%) eyelids of 124 (14.3%) patients</p>		<p>and that operated on by the IECWs was not statistically significant (P=0.24)</p>
8	(Burton, Kinteh, et al., 2005)	The Gambia	<p>Objective: To investigate whether enhanced control of infection, both of Chlamydia trachomatis and other bacteria, with azithromycin can improve surgical outcome in a trachoma control Programme</p> <p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: Azithromycin - Control group: Tetracycline eye ointment <p>Procedure/s: PLTR</p>	<p>6 months and 1 year</p> <p>Follow up rates: At 6 months – 410/451 (91%) patients 1 year – 426/451 (94%) patients</p>	<p><u>At 6 months:</u> 129/410 (31.5%)</p> <ul style="list-style-type: none"> - Azithromycin group - 74/199(37.2%) - Control group 55/211(26.1%) <p><u>At 1 year:</u> 176/426 (41.3%) had one or more lashes touching the eye</p> <ul style="list-style-type: none"> - Azithromycin group – 84/204(41.2%) 	<p>At 1 year:</p> <ul style="list-style-type: none"> - There was 1 chlamydial infection in the azithromycin group and 3 in the control group. - 27 individuals had developed new corneal opacification (CC2 or CC3), of whom 14 	<p><u>Associated risk factors:</u> Post-operative trichiasis was significantly associated with more severe preoperative trichiasis, bacterial infection, and severe conjunctival inflammation at 12 months. Significant variability in outcome was found between surgeons (total range: 0-83%)</p>

			<p>Number of participants/eyelids: 451 people with TT; 216 to azithromycin group and 235 to the control group</p> <p>Primary outcome measure: Post-operative trichiasis (one or more lashes touching the eye)</p>		Control group 92/222(41.4%)	<p>(52%) had no post-operative trichiasis.</p> <ul style="list-style-type: none"> - Visual acuity improved in 57.6% and deteriorated in 28.4% of eyes by 12 months. 	
11, 28	<p>(Burton et al., 2012)</p> <p>(Rajak et al., 2011a)</p>	Ethiopia	<p>Objective: To investigate whether using absorbable sutures instead of silk sutures might reduce the risk of post-operative disease among patients with major trichiasis.</p> <p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: Absorbable sutures - Control group: Silk sutures <p>Procedure/s: PLTR</p> <p>Number of participants/eyelids: 1,300 individuals with major trichiasis (650 in the absorbable suture group and 650 in the silk sutures group)</p> <p>Primary outcome measure: the proportion of those individuals seen at the 12-months follow-up who were found to have either post-operative trichiasis, defined as one or more lashes touching the eye or clinical evidence of</p>	<p>1 year</p> <p>Follow up rates: 1236/1300 (95%) patients were seen (608 in intervention group and 628 in control group)</p>	<p>234/1236 (19%) participants/study eyes developed post-operative trichiasis within the first year of the trial</p> <p>114 [18.2%] in the absorbable suture group versus 120 [19.7%] in the silk suture group.</p>	<p>Granuloma – Absorbable suture group (5.7%), silk suture group (8.7%)</p> <p>Notching – 14% in absorbable suture group and 11.9% in the silk suture group</p>	<p>There was no evidence that use of absorbable polyglactin-910 sutures was associated with a lower incidence of post-operative trichiasis 1-year post surgery than silk sutures.</p> <p><u>Associated risk factors:</u> Post-operative trichiasis at both 1 and 2 year was significantly associated with both more severe entropion at baseline and baseline conjunctival inflammation.</p>

			epilation, or a history of repeat TT surgery during the first year.				
13, 32 33,35	(Gower et al., 2011) (West et al., 2006) (West et al., 2007) (Woreta et al., 2012)	Ethiopia	<p>Objective:</p> <p>1) To determine if postoperative treatment with azithromycin compared with topical tetracycline reduces the incidence of post-operative trichiasis up to 1 year and if azithromycin treatment of household members provides additional benefit compared with treating only the surgical patient.</p> <p>2) To evaluate risk factors for early trichiasis recurrence and other unfavourable short-term outcomes</p> <p>Design: RCT with 3 study arms</p> <ul style="list-style-type: none"> - Arm A - single-dose (1 g) oral azithromycin alone - Arm B - single-dose azithromycin for patient and household members (20 mg/kg up to 1 g) - Arm C - Topical tetracycline (twice per day for 6 weeks). <p>Procedure/s: BLTR</p> <p>Number of participants/eyelids: 1452 patients presenting for first-time trichiasis surgery. Patients were randomized 1:1:1 to the 3 study arms i.e. 483 to 485 in each</p>	<p>6 weeks, 1 year and 3 years</p> <p>Follow up rates: At 6 weeks – 1449/1452 (99.8%) patients</p> <p>At 1 year 97% (1414/1452) patients</p> <p>At 3 years Retention rate was >90% in each study arm</p>	<p><u>At 6 weeks</u> At 6 weeks – 59/2610 (2.3%) eyelids had post-operative trichiasis</p> <p><u>At 1 year</u> Cumulative incidence– 107/1414 (7.6%) patients</p> <p>Arm A - 26/472 (5.5%) Arm B – 36/472 (7.6%) Arm C – 45/470 (9.6%)</p> <p>The incidence of post-operative trichiasis was lower in the azithromycin group (A + B) compared to the topical tetracycline group (C): 6.9/100-person years vs 10.3/100 person-years (P 5 0.047), respectively</p>	<p>35/2610(1.3%) had an eyelid closure defect.</p> <p>22/1881(1.2%) had eyelid contour abnormalities</p> <p>98/1881(10.5%) had pyogenic granuloma formation</p>	<p>Associated risk factors:</p> <p><u>At 6 weeks:</u></p> <ul style="list-style-type: none"> - Surgeon-related factors were predictive of eyelid closure defect and granuloma formation. - Eyelids with short incisions were nearly four times more likely to have post-operative trichiasis - Baseline trichiasis severity was predictive of eyelid contour abnormalities and post-operative trichiasis. - Epilation was associated with granuloma formation but was protective against eyelid closure defect. <p><u>At 1 -year</u></p> <ul style="list-style-type: none"> - Male sex - Moderate/severe pre-operative entropion

			<p>arm. For patients with bilateral TT, 1 eye was selected for inclusion in the study</p> <p>Primary outcome measure: post-operative trichiasis (the presence of one or more lashes touching the globe and/or evidence of epilation confirmed by questioning the patient)</p>		<p><u>At 3 years:</u> Cumulative: 12%; 10% in the azithromycin group; 13% in the topical tetracycline group</p>		<p>- No azithromycin treatment - Incision <22 mm</p> <p><u>At 3 years:</u> - Severity of entropion prior to surgery - Male sex</p>
14	(Gower et al., 2013)	Tanzania	<p>Objective: To determine whether a new surgical clamp (TT clamp) reduces unfavourable postoperative outcomes compared to the standard BLTR instrumentation</p> <p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: BLTR procedure with the TT clamp - Control group: Standard BLTR <p>Procedure/s: BLTR</p> <p>Number of participants/eyelids: 3345 eyes of 1917 Patients with previously unoperated TT</p> <p>Primary outcome measure: Post-operative trichiasis defined as 1 or more eyelashes touching or evidence of epilation</p>	<p>2 years</p> <p>Follow up rates: 3343/3345 (99.9%) eyelids</p>	<p>Overall incidence– 1333/3343 (39.9%) eyelids</p> <ul style="list-style-type: none"> - TT clamp group – 721/1669 (43.2%) - Standard BLTR group – 612/1674 (36.6%) 	<p>Granulomata - TT clamp (16.8%), standard BLTR group (22.4%)</p> <p>ECAs - TT clamp Group (16.3%), standard BLTR group (23.7%)</p>	<p>This randomized clinical trial found similar overall rates of unfavourable outcomes between the TT clamp and standard BLTR groups (60.9% vs 63.0%, respectively).</p> <p>Postoperative TT was more common in the TT clamp group than in the standard BLTR group (43.2% vs 36.6%, respectively, by 24 months)</p>
15,29	(Habtmu et al., 2015)	Ethiopia	<p>Objective: To compare the long-term impact of trichiasis surgery versus repeated epilation in</p>	<p>2 years and 4 years</p>	<p><u>At 2 years</u> Overall, 412/1216 (33.9%) patients</p>	<p>Lid margin conjunctivalisation was higher in the</p>	<p>There were no differences between participants in the</p>

	(Rajak et al., 2011b)		<p>preventing visual impairment and corneal opacity from TT</p> <p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: PLTR - Control group: Repeated epilation <p>Procedure/s: PLTR and repeated epilation</p> <p>Number of participants/eyelids: 1300 individuals with minor TT</p> <p>Primary outcome measure: Post-operative trichiasis defined as one or more lashes touching the eye or history of surgery/repeat surgery in the trial eye</p>	<p>Follow up rates:</p> <p>At 2 years - 1216/1300 (93.5%)</p> <p>At 4 years – 1151/1300 (88.5%)</p>	<p>Surgery group – 114/613 (17.5%)</p> <p>Epilation group – 298/603 (49.4%)</p> <p><u>At 4 years:</u></p> <p>Overall – 340/1151 (29.5%) patients</p> <p>Surgery arm – 122/579 (21.1%)</p> <p>Epilation-to-surgery arm – 42/198 (22.2%)</p> <p>Epilation only – 176/383 (45.9%)</p>	epilation-only group	<p>epilation-only, epilation-to-surgery and surgery arm participants in changes in visual acuity and corneal opacity between baseline and four-years.</p> <p>Independent risk factors for 5+ lashes touching were baseline age ≥ 50 years, ≥ 3 lashes at baseline, and infrequent epilation</p>
16, 17,18	<p>(Habtamu et al., 2016)</p> <p>(Habtamu et al., 2017a)</p> <p>(Habtamu et al., 2017b)</p>	Ethiopia	<p>Objective: To compare the outcomes of PLTR and BLTR surgery for TT</p> <p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: PLTR - Control group: BLTR <p>Procedure/s: PLTR and BLTR</p> <p>Number of participants/eyelids: 1000 participants with trichiasis (501 in the BLTR group and 499 in the PLTR group)</p> <p>Primary outcome measure: cumulative proportion of</p>	<p>1 year</p> <p>Follow up rates: 981/1000 (98%).</p> <p>Data on post-operative trichiasis were available for 992/1000 (99.2%) participants, 496 in each arm, who were reassessed on at least 1 occasion during the 12-month period</p>	<p>Cumulative incidence at 12 months: Overall – 173/992 (17.4%) patients</p> <p>PLTR group – 63/496 (13%)</p> <p>BLTR group – 110/496 (22%)</p>	<p>Granulomata: PLTR – 5.2%, BLTR – 2.2%</p> <p>ECA's – PLTR – 6.3%, BLTR – 7.6%</p>	<p>Post-operative trichiasis was lower in the PLTR group compared to the BLTR group.</p> <p><u>Associated risk factors:</u></p> <p>Poor postoperative outcomes in TT surgery were associated with inadequate peripheral dissection, irregular incision, asymmetric suture position and</p>

			individuals who developed post-operative trichiasis (1 or more lashes touching the eye or evidence of epilation or history or repeat surgery) by 12 months				tension, inadequate correction, and lash location.
19	(Habtamu et al., 2018)	Ethiopia	<p>Objective: To investigate whether doxycycline might reduce the risk of postoperative trichiasis following surgery in patients with trichomatous trichiasis through anti-matrix metalloproteinase and anti-inflammatory activity</p> <p>Design: RCT</p> <ul style="list-style-type: none"> - Intervention group: Oral doxycycline - Control group: placebo <p>Procedure/s: PLTR</p> <p>Number of participants/eyelids: 1000 patients with upper lid trichomatous trichiasis in association with tarsal conjunctive scarring ((499 patients to doxycycline, 501 patients to placebo)</p> <p>Primary outcome measure: cumulative proportion of individuals who developed postoperative trichiasis (1 or more lashes touching the eye) by 12 months.</p>	<p>1 year</p> <p>Follow up rates: 999/1000 (99.9%) patients; 498 in the doxycycline group and 501 in the placebo group</p>	<p>Overall – 120/999 (12%) patients developed post-operative trichiasis</p> <p>58 of the 498 patients (12%) in the doxycycline group and 62 (12%) of 501 patients in the placebo group had developed postoperative trichiasis</p>	None	Doxycycline did not reduce the risk of postoperative trichiasis and is therefore not indicated for the improvement of outcomes following trichomatous trichiasis surgery

Appendix 2: Observational studies

Study ID	Study author, year	Country	Study characteristics	Follow up period	Results		Risk factors
					Post-operative trichiasis	Other poor outcomes	
2	(Ahmed & Abdelbaky, 2015)	Egypt	<p>Objective: To evaluate the outcome of anterior lamellar reposition (ALR) in treating trachomatous trichiasis.</p> <p>Design: Prospective non-comparative study/ clinical trial</p> <p>Procedure/s: ALR</p> <p>Number of participants/eyelids: 752 eyelids of 445 patients with trachomatous trichiasis or entropion with short or thin tarsus</p> <p>Primary outcome measure: Post-operative trichiasis defined as presence of 1 or more lashes touching the globe</p>	<p>3 weeks, 3 months and 6 months</p> <p>Follow up rate: 100%</p>	<p><u>At 3 weeks</u> 69.2% (520 lids) developed post-operative trichiasis; 2.66% (20) eyelids had ≥ 6 lashes</p> <p><u>At 3 months</u> 336/752 (44.7%) eyelids had post-operative trichiasis; of these, 11.3% lids had ≥ 6 lashes</p> <p><u>At 6 months</u> 255/752 eyelids (33.9%) had post-operative trichiasis; of these 112 (14.9%) had ≥ 6 lashes</p>	<p>Local madarosis developed in 5.72% of the operated eyelids by the end of the follow up period</p>	<p>By the end of the follow-up period, severe post-operative trichiasis incidence (≥ 6 lashes) was reported in 112 lids (14.9%) and was considered to be failure being in need for another surgery.</p>
4	(Assefa et al., 2008)	Ethiopia	<p>Objective: To evaluate the post-operative outcome of posterior tarsal rotation done by integrated eye care workers (IECWs) at the twelfth postoperative month</p> <p>Design: Prospective study</p>	<p>1 year</p>	<p>77 (21.3%) of the 361 patients were found to have post-operative trichiasis in one or both of the operated eyes</p>	<p>None</p>	<p><u>Associated risk factors:</u> There was an increase in likelihood of suffering post-operative trichiasis with increasing age of patients. A statistically</p>

			<p>Procedure/s: transverse tarsotomy with lid margin rotation (TTR)</p> <p>Number of participants/eyelids: 695 eyelids of 455 patients with trichiasis</p> <p>Primary outcome measure: Post-operative trichiasis defined as one or more eyelashes touching the globe or history of epilation after surgery.</p>	<p>Follow up rate: 79.3% (361/455) patients</p>	<p>In terms of eyelids, 93 of the 560 (16.6%) operated lids upper eyelids.</p>		<p>significant difference in the incidence of post-operative trichiasis among patients operated by different surgeons was also reported.</p>
5	(Bog, Yorston & Foster, 1993)	Tanzania	<p>Objective: To assess the results of community-based eyelid surgery for trichiasis due to trachoma.</p> <p>Design: Prospective community-based study</p> <p>Procedure/s: Tarsal plate rotation</p> <p>Number of participants/eyelids: 156 eyelids of 94 patients with trichiasis due to trachoma</p> <p>Primary outcome measure: Success defined as no lashes touching the globe in any position after surgery</p>	<p>Mean 25.5 months (9-36 months)</p> <p>Follow up rates: 144/156 eyelids of 86 patients (92.3%)</p>	<p>Cumulative incidence of post-operative trichiasis at the last follow up was 17.4%.</p>	<p>1 eye developed a wound infection 9 eyes (6.3%) developed minimal central notching of the upper eyelid within the follow up period.</p>	<p>Survival time analysis showed a probability of survival without post-operative trichiasis of 81% at 24 months and 79% at 36 months.</p>

6	(Bouazza et al., 2017)	Ethiopia	<p>Objective: To assess functional and aesthetic results of anterior lamellar resection with lid margin splitting of the upper lid in the treatment of cicatricial trichomatous entropion</p> <p>Design: Descriptive cross-sectional study</p> <p>Procedure/s: Anterior lamellar resection with lid margin splitting</p> <p>Number of participants/eyelids: 26 patients with cicatricial trichomatous entropion</p> <p>Primary outcome measure: Success (no lashes in contact with the cornea) and no associated eyelid complications</p>	6 months	During the follow-up period, no cases of post-operative entropion were reported.	In 3 patients, a residual contact of one or a few eyelashes (<5 eyelashes) persisted. These three patients required a complementary treatment such as argon laser.	Correction of the cicatricial entropion was achieved in 24 patients (92.3% of cases) and full correction of misdirected lashes without any contact with the ocular surface was obtained in 23 patients (88.4% of cases). The lid margin was regular in 88.4% of cases. A significant improvement of the tear film and corneal surface was observed in 84.6% of patients.
7	(Bowman et al., 2000)	The Gambia	<p>Objective: To assess the long-term follow-up of lid surgery for trichiasis in the Gambia: surgical success and patient perceptions</p> <p>Design: Retrospective Cross-sectional study</p> <p>Procedure/s: Lid surgery (Tarsal rotation procedure)</p>	Median time since surgery was 7 years	63/115 (55%) operated eyes in 42/65 (65%) people had suffered post-operative trichiasis.	4 of 115 operated eyes (3.5%) had inadequate lid closure and corneal exposure. 3 of these had central corneal opacity.	

			<p>Number of participants/eyelids: 115 eyes of 65 patients who had undergone trichiasis surgery</p> <p>Primary outcome measure: Post-operative trichiasis (one or more lashes).</p>				
9	(Burton, Bowman, et al., 2005)	The Gambia	<p>Objective: To assess the long-term outcome of surgery and its effect on vision and corneal opacification</p> <p>Design: Retrospective cohort study Procedure/s: Posterior lamellar tarsal rotation (PLTR)</p> <p>Number of participants/eyelids: 162 individuals who had undergone trichiasis surgery in 1998</p> <p>Primary outcome measure: Post-operative trichiasis - one or more lashes touching the eye</p>	Mean: 3.5 years (range: 2.9–4.5 years)	At follow up 89/214 (41.6%) previously operated eyes had suffered post-operative trichiasis; 52/214 (24.3%) had five or more lashes touching the eye, including those with extensive epilation.	General deterioration in visual acuity between surgery and follow up, which was greater if new corneal opacification developed or trichiasis returned.	<u>Associated Risk factors:</u> Post-operative trichiasis was associated with conjunctival Inflammation. Bacterial infection was also independently associated with post-operative trichiasis following surgery
10	(Burton et al., 2010)	The Gambia	<p>Objective: To explore immunopathogenic factors that may be involved in the recurrence of TT after tarsal rotation surgery.</p> <p>Design: Prospective cohort study Procedure/s: PLTR</p>	4 years after surgery Follow up rates: At 4 years 194/240, (80.8%) individuals were reassessed.	Of the 194 individuals examined at both 1 and 4 years after surgery, 117 did not have post-operative trichiasis at 1 year. By 4 years, 24 (20%) of these 117	Other poor outcomes: At 1-year, tarsal conjunctival inflammation (P2/P3) was observed in 91	<u>Associated risk factors:</u> - Post-operative trichiasis was associated with a reduced MMP-1 to TIMP-1 ratio, which may favour the accumulation of fibrotic tissue.

			Number of participants/eyelids: 240 individuals selected from 451 individuals who had undergone trichiasis surgery 1 year earlier. Primary outcome measure: Post-operative trichiasis (one of more lashes touching the globe)		people had incident post-operative trichiasis.	(38%) of 240 study eyes	Non-chlamydial bacterial infection may induce factors that contribute to conjunctival tissue remodelling and post-operative trichiasis in trachoma.
12	(el Toukhy, Lewallen & Courtright, 2006)	Egypt	Objective: To determine the early success and failures of Bilamellar tarsal procedure in trichomatous trichiasis Design: Prospective study Procedure/s: BLTR Number of participants/eyelids: 638 lids of 493 patients with unoperated trichiasis Primary outcome measure: Surgical failure defined as one or more lashes touching the eyeball.	8 to 10 weeks over a 4-year study period Follow up rates: 599/638 (94%) lids	98/599 (16.4%) lids	None	<u>Associated risk factors:</u> - Failure was associated with pre-operative corneal staining), pre-operative corneal opacity, the use of silk sutures and the use of 4 or more sutures.
20	(Kerie & Bejiga, 2010)	Ethiopia	Objective: To assess the incidence of post-operative TT 3 months after trichiasis surgery Design: Cross sectional survey Procedure/s: BLTR Number of participants/eyelids: 1317 eyelids of 780 patients	3 months	238/780 (30.5%) by person 308/1317 (23.4%) by eyelids	Conjunctival and eye lid inflammation – 32.4%	

			Primary outcome measure: Post-operative trichiasis (one of more lashes touching the globe)				
21	(Khafagy, Mostafa & Fooshan, 2012)	Egypt	<p>Objective: To evaluate the outcome of combined eyelid splitting with selective cryotherapy to the anterior lid lamella for treating a trichiasis-involved large segment of the lid margin.</p> <p>Design: Prospective study Procedure/s: combined eyelid splitting and selective cryotherapy</p> <p>Number of participants/eyelids: 20 eyelids of 10 patients</p> <p>Primary outcome measure: Post-operative trichiasis (one of more lashes touching the globe).</p>	6 months Follow up rates: 100%	2/20(10%) eyelids of 2 patients developed post-operative trichiasis	Mild lid edema occurred in all patients postoperatively, which resolved within 1 week.	
22,31	(Merbs, West & West, 2005) (West et al., 2005b)	Tanzania	<p>Objective: To evaluate the pattern of post-operative trichiasis after BLTR surgery for trachoma.</p> <p>Design: Observational cohort (Retrospective)</p> <p>Procedure/s: BLTR Number of participants/eyelids: 630 eyes of 384 patients having at least 1 eye that had undergone TT surgery a minimum of 18 months before the study commencement</p>	> 18 months	176/630 (28%) eyes developed post-operative trichiasis	None	<p>Post-operative trichiasis after surgery is more common in the left eye and on the left side of the eyelid. The surgical procedure is more difficult to perform on the right side of the eyelid by a right-handed surgeon.</p> <p><u>Associated risk factors:</u></p>

			Primary outcome measure: Post-operative trichiasis defined as one or more lashes touching the globe after surgery.				Post-operative trichiasis was associated with tarsal conjunctival inflammation and residence in the Kongwa district.
23	(Merbs et al., 2015)	Tanzania	<p>Objective: To investigate the relationship between postoperative scar height and surgical success of the Bilamellar tarsal rotation (BLTR) procedure, commonly used to correct trichiasis secondary to trachoma</p> <p>Design: Preliminary data analysis from the PRET trial</p> <p>Procedure/s: BLTR</p> <p>Participants: 145 sequential participants (245 eyelids) at their 1-year postoperative visit were examined</p> <p>Primary outcome measure: Post-operative trichiasis defined as one or more lashes touching the globe after surgery.</p>	1 year	77/245 (31%) eyelids had postoperative trichiasis	None	Internal scar height <4.5mm measured 1 year after surgery is more likely to be associated with postoperative trichiasis. WHO recommends an incision height of 3.0mm, as the optimum incision height to minimize postoperative trichiasis
24	(Ndoye et al., 1997)	Senegal	Objective: Trachomatous entropion trichiasis at the	2 years	Incidence rates: 17.6% over a 2-year period	None	

			<p>ophthalmologic clinic of Dantec CHU</p> <p>Design: Retrospective study Procedure/s: Trabut/ PLTR</p> <p>Number of participants/eyelids: 199 eyes of 137 patients</p> <p>Primary outcome measure: Post-operative trichiasis defined as one or more lashes touching the eyeball.</p>				
25	(Négrel et al., 2000)	Morocco	<p>Objective: To assess the quality of trichiasis surgery</p> <p>Design: Cross-sectional survey Procedure/s: BLTR</p> <p>Number of participants/eyelids: 740 people chosen from the surgical records of 13 health centres of the provinces of Zagora and Errachidia (Kingdom of Morocco)</p> <p>Primary outcome measure: Post-operative trichiasis defined as presence of at least one or more eyelashes in contact with the eyeball.</p>	Over 6 months	Incidence rates: 117 of 740 (15.8%) patients developed post-operative trichiasis	<ul style="list-style-type: none"> - Overcorrection: 2.3% (17/740) - Ptosis: 0.4% (3/740) - Lid necrosis without corneal exposure: 3.6% (27/740) - Lid necrosis with corneal exposure: 0.14% (1/740) - Granuloma: 0.95% (7/740) 	<u>Associated risk factors:</u> Age (over 40 years), having been operated on in Errachidia province, having been operated on by a general practitioner or by an ophthalmologist.

26	(Pearson et al., 2013)	Ethiopia	<p>Objective: To evaluate the outcomes of community-based trichiasis surgery with absorbable sutures, conducted in Amhara Regional State, Ethiopia</p> <p>Design: Cross-sectional survey Procedure/s: BLTR</p> <p>Number of participants/eyelids: 363 patients who had undergone TT surgery in eye camps between October 2005 and August 2006.</p> <p>Primary outcome measure: Post-operative trichiasis defined as presence of at least one or more eyelashes in contact with the eye.</p>	~11 months	34/363 (9.4%) patients	Granuloma 0.6%; lid closure defects 5.5% and lid notching 16.8%.	Prevalence of post-operative trichiasis and granuloma were lower than expected but higher for lid closure defects and lid notching, compared to other studies that have described prevalence ranging from 10.8% to 61.8%.
27	(Rajak et al., 2010)	The Gambia	<p>Objective: To investigate the incidence of post-operative trichiasis after surgery.</p> <p>Design: Prospective study Procedure/s: PLTR</p> <p>Number of participants/eyelids: 356 trichiasis patients Primary outcome measure: Post-operative trichiasis, defined as one or more lashes touching any part of the globe in primary position.</p>	4 years 266/356 (74.7%) patients were reassessed at 4 years	4 years – 41% 110 (41%) of 266 study eyes 4 years after surgery. This result compares with 32% at 6 months and 40% at 1 year	At 4 years, 98 (36%) study eyes had visually significant Corneal opacity.	<p>Incidence of post-operative trichiasis was high, and most cases recurred within 6 months of surgery.</p> <p>Post-operative trichiasis was associated with severe conjunctival inflammation and severe trichiasis (≥ 10 lashes) at baseline.</p>
30	(Rajak et al., 2013)	Ethiopia	Objective: To investigate the incidence of post-operative	2 years	Overall, post-operative trichiasis	Within 2 years, Granuloma	Baseline disease severity and inter-

			<p>trichiasis, other complications and factors associated with poor outcomes after surgery</p> <p>Design: Prospective Procedure/s: PLTR</p> <p>Number of participants/eyelids: 1300 patients previously unoperated trichiasis in at least one eye</p> <p>Primary outcome measure: post-operative trichiasis defined as either (1) one or more eyelashes touching the eye or (2) clinical evidence of epilation.</p>	<p>Follow up rates: At 2 years, 1276/1300 (98.2%) participants were re-examined</p>	<p>occurred in 315/1276 (24.7%) study eyes within the 2 years</p>	<p>occurred in 69 (5.7%) and notching in 156 (13.0%).</p>	<p>surgeon variation are major determinants of post-operative trichiasis.</p>
34	(Woreta et al., 2009)	Ethiopia	<p>Objective: To determine the effect of trichiasis surgery on visual acuity.</p> <p>Design: Prospective study within the STAR trial Procedure/s: BLTR</p> <p>Number of participants: 790 eyes of 448 patients</p> <p>Primary outcome: visual acuity Secondary outcome: Post-operative trichiasis defined as one or more lashes touching the globe after surgery.</p>	<p>6 months</p> <p>Follow-up rate: 439/448 (98%)</p>	<p>36/790 (4.6%) operated eyelids developed post-operative trichiasis</p>	<p>Pain – 1.4% Photophobia – 0.9%</p>	<p>Only 36 of the 790 eyes that had surgery developed post-operative trichiasis, the power of the study to detect change in visual effect for eye that developed post-operative trichiasis was limited.</p>

Manuscript 2

Post-operative trichomatous trichiasis in Africa: An online survey of national approaches to surgical follow up, outcome assessment, and audit in trachoma-endemic countries in Africa

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ABSTRACT

Background

Current evidence suggests that poor outcomes of trichiasis surgery, including post-operative trichiasis and other complications, remain common in most trachoma-endemic countries in Africa. To improve this situation, the World Health Organization recommends regular follow up, outcome assessment and audit of trichiasis surgeons.

Methods

We sought to assess the national policies and strategies regarding trichiasis surgical follow up, outcome assessment and audit of trichiasis surgeons using an online survey questionnaire administered in [month, year] all trachoma-endemic countries in Africa.

Results

All national programmes provided information; 2 of the 29 had not yet implemented trichiasis surgery as part of their trachoma elimination programme so we have findings from 27 countries. Only four countries reported having a national policy for trichiasis surgery follow up and outcome assessment and only two had a national policy for conducting an audit of trichiasis surgeons. In addition, 18 of the 27 countries surveyed did not have a cut-off point at which poorly performing surgeons would be instructed to discontinue surgery until retraining or other interventions had been undertaken.

Discussion

Trachoma programmes in Africa are faced with a myriad of challenges that deter them from managing the outcomes of trichiasis surgery effectively. These include lack of policies and systems to track and monitor outcomes of trichiasis surgery, low post-operative follow-up of trichiasis patients, which makes the monitoring of outcomes and provision of post-operative care difficult, and limited research on the burden of post-operative trichiasis to inform planning. To address the growing challenge of post-operative trichiasis and other poor outcomes, there is need for national trachoma programmes to put in place policies and strategies, systems and structures to follow up patients, assess surgical outcomes and monitor the performance of individual surgeons through surgical audits and supportive supervision. In future, the new TT tracker tool may assist national trachoma programmes to track TT patients for surgical follow up, outcome assessment and audit of trichiasis surgeons.

INTRODUCTION

Preliminary analysis of population-based data from the Global Trachoma Mapping Project indicates that, varying by location, 10-75% of people who currently have trichiasis have already had trichiasis surgery (World Health Organization, 2016). This number may change with increasing output of trichiasis surgery programmes in trachoma-endemic countries (World Health Organization, 2016).

WHO recommends regular follow up of patients and monitoring of trichiasis surgery outcomes as a way of reducing post-operative trichiasis (World Health Organization, 2016). According to the *Trachoma Control: A Guide for Programme Managers* (World Health Organization, 2006), all operated trichiasis patients should be seen on the first post-operative day for eye patch removal and examination of the wound. A follow-up assessment at 8 to 14 days is recommended; essential if non-absorbable sutures were used to remove the sutures and inspect the wound (World Health Organization, 2016). All TT patients should be followed up for at least 3 to 6 months after surgery (World Health Organization, 2016). During every follow-up visit, both eyes examined for post-operative trichiasis in the operated eye or new TT in an unoperated eye. The primary goal of outcome assessment is for the surgeon to assess the status of the eye and patient and make decisions regarding further management.

An additional, parallel approach to improve outcomes of trichiasis surgery is through audit of trichiasis surgeons and supportive supervision. According to a report of the WHO GET2020 Second Global Scientific Meeting on Trachomatous Trichiasis held in 2015, programmes should assess a sample of surgeries for each surgeon individually for audit purposes. This data should then be used to review the performance of new trichiasis surgeons 3 to 6 months after certification, and of existing trichiasis surgeons annually (World Health Organization, 2016). If a surgeon is found to have an unacceptably high proportion of post-operative trichiasis and other poor outcomes above the pre-determined threshold, re-training and supportive supervision by a more experienced surgeon is recommended (Buchan, Limburg & Burton, 2011; Courtright, Burton & Emerson, 2012; Merbs et al., 2015).

Anecdotally, however, successful implementation of patient follow up, monitoring of patient outcomes and auditing of surgeons' performance are very challenging for trachoma programmes (World Health Organization, 2016). National programmes are believed to lack effective routine systems and policies for monitoring outcomes and conducting surgical audits. Patients are often lost to follow up after surgery which makes providing post-operative care and monitoring of outcomes difficult (International Coalition for Trachoma Control, 2015).

We undertook an online survey to assess the availability of national policies and strategies for monitoring outcomes and for conducting surgical audits, and strategies for addressing poor surgical

Study design

This cross-sectional design online survey was carried out between May and July 2018. An online survey questionnaire was used to collect information on the national targets for surgical outcomes, policies and monitoring, and strategies to address poor performance by surgeons. The survey questionnaire was piloted on the target population to assess the participants' views on the wording, content and format of the questionnaire. Feedback from this pre-test was incorporated in the development of the final iteration of the questionnaire. The final questionnaire was then translated into French and Portuguese for non-English speaking countries and validated to ensure that the translated measure was equivalent to the original questionnaire.

Ethics statement

Ethical approval for the study was obtained from the University of Cape Town Health Sciences Research Committee and the WHO Ethics Review Committee (0003034).

Data Processing and Analysis

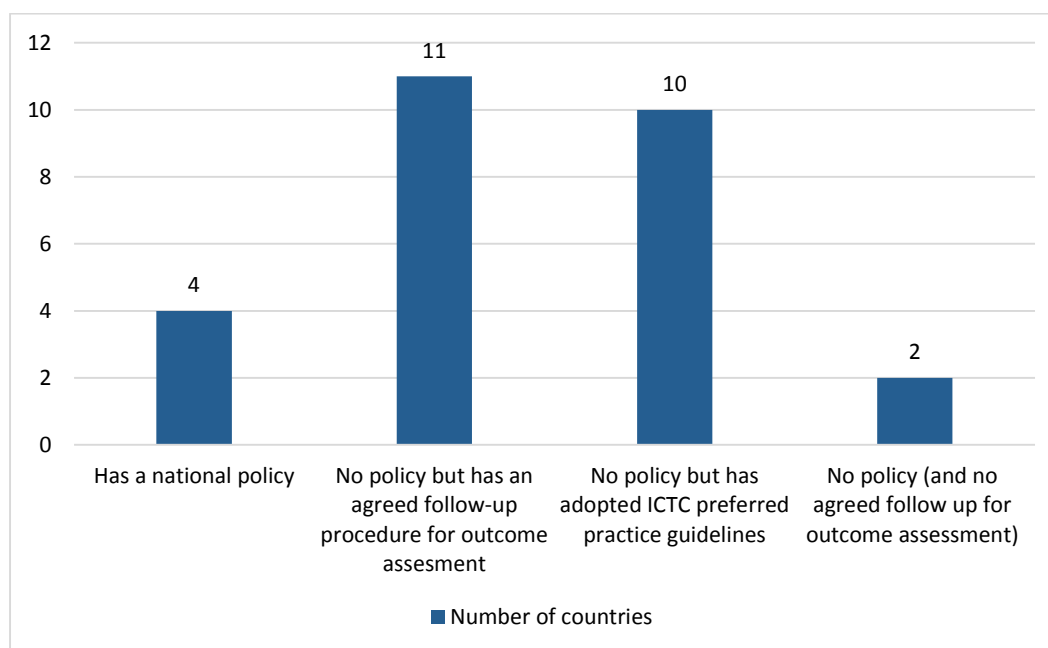
The survey results were entered into Microsoft Excel, checked for completeness and verified against the original response forms. All the responses that were in French and Portuguese were then translated into English and checked for correctness. Aggregated tables, as well as pie and column charts were then generated to represent results using advanced Excel. Qualitative data was analysed using thematic analysis and narrative synthesis in line with the study objectives.

RESULTS

The survey was conducted between May and July 2018. Two of the 29 trachoma-endemic countries in WHO African region where this survey was conducted had not started implementing the “surgery” part of the SAFE strategy and did not have policies or systems in place for surgical follow up, outcome assessment and audit of trichiasis surgeon. Therefore, the two were excluded from data analysis, as the survey questions were not applicable to them, thereby reducing the number of surveyed countries to 27.

Post-operative follow-up and outcome assessment

Among the 27 countries involved in this survey, only four reported having a national policy for follow-up of trichiasis patients after surgery– Figure 2. Of the remaining 23, 11 countries did not have national policies or guidelines but have put in place systems and structures for follow up of patients trichiasis after surgery, 10 countries have adopted the ICTC preferred practice guidelines and two countries had no policy and no agreed follow up procedure for outcome assessment.

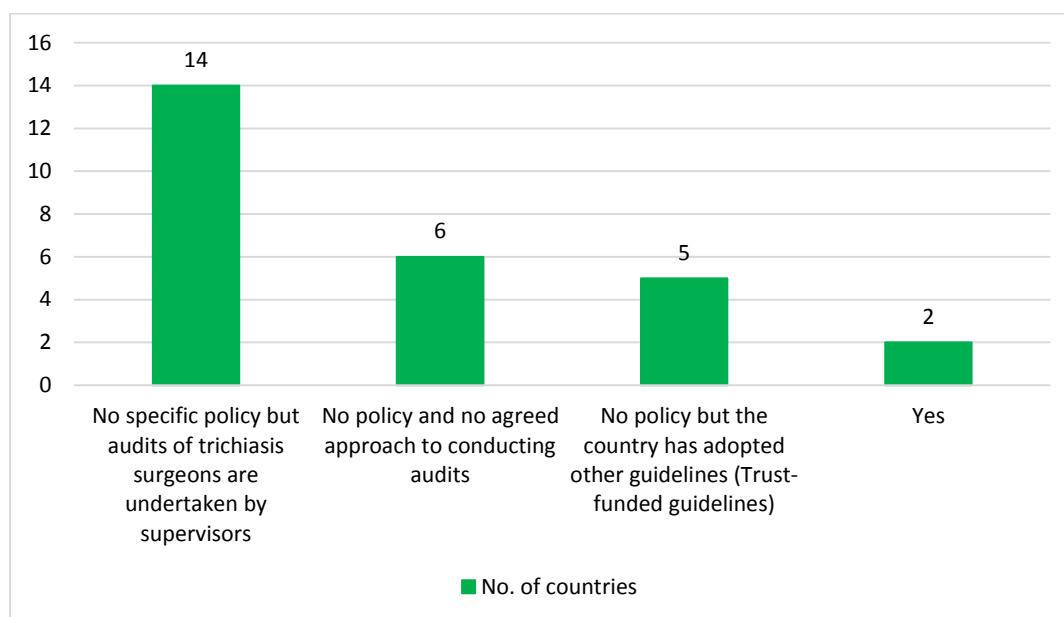
Figure 2. Availability of a national policy for trichiasis surgery follow-up

16 of the 27 countries surveyed reported having three recommended follow up periods as part of their national policy or guidelines: 1-day post-operative follow-up, at 1-2 weeks to remove sutures and last follow up either at 3-6 months or 1 year after surgery. Of the remaining 11 countries, 4 countries had at least two follow up periods ranging from 1-day post-operatively to 1-year after surgery, 6 countries had only one recommended follow up period either at 1-2 weeks or at 3-6 months, and 1 country did not have any recommended follow up period for patient re-examination after surgery. Overall, all but 3 countries reported having a scheduled follow up at 3-6 months after surgery.

89% (24 of 27 countries) involved in this survey reported having a set national target for good surgical outcomes which is defined as the percentage of trichiasis surgeries that the country seeks to have recorded as a good outcome [no post-operative trichiasis] at 3-6 months or the last routine time that follow up is scheduled. Out of the 24, 3 countries reported having a target of 100% good outcomes, 14 countries had a target of 90% success rate (or less than 10% cases of post-operative trichiasis), 6 countries had a target of 80% good outcomes and 1 country had a target of 85% success rate. Three of the 27 countries surveyed had not set any national targets for good outcomes.

Surgical audits

For surgical audits, only two countries reported having a national policy to guide the assessment of surgical outcomes of their surgeons. Most of the countries surveyed, 19 of the 27 countries, had no specific government policy but reported that audits of trichiasis surgeons were undertaken by supervisors (n=14) or had adopted other guidelines, such as the Queen Elizabeth Diamond Jubilee Trust funded surgical audit guidelines (n=5). The remaining six countries had no policy and no agreed approach to conducting audits – Figure 3.

Figure 3. Countries with a national policy for conducting surgical audit

To improve surgeons' performance and quality of surgery, WHO recommends that surgeons with poor outcomes above the agreed threshold should discontinue surgery until retraining or other interventions have been undertaken. In this survey, only 10 of the 27 countries surveyed reported having a nationally accepted cut-off point (percentage of post-operative trichiasis by a surgeon) at which a surgeon should discontinue surgery until retraining or other interventions have been undertaken. Variable cut-off points were reported among the 10 countries; 30% poor outcomes (3 countries), 25% (1 country), 20% (4 countries), 15% (1 country) and 10% (1 country). Of the remaining 17 countries, three reported having a system whereby trichiasis surgeons with consistent poor outcomes were required to stop performing surgery until they are retrained, but they did not have a specific percentage or cut-off point for that. The other 14 countries do not have cut-off points at which a surgeon should discontinue surgery.

Management of post-operative trichiasis

Current approaches for managing post-operative trichiasis

Different countries use different approaches to manage post-operative trichiasis. In 13 of the 27 countries, cases of post-operative trichiasis and other poor outcomes are managed by another trichiasis surgeon who is more experienced. In other countries, these cases are managed by a specially trained ophthalmologist (n=6 countries) or by the same surgeon who performed the first procedure (n=7 countries). One country did not specify its current approach for managing post-operative trichiasis. Other approaches used to manage post-operative trichiasis in trachoma-endemic countries in Africa include referral to secondary eye units; managed by the surgeon that identifies them during a surgical campaign, since the patient may have returned for a second surgery.

Although responsibility for managing post-operative trichiasis lies with the national trachoma programmes, this survey brought out scores of challenges that these programmes face which may deter their ability to reduce and manage post-operative trichiasis. Some of the key challenges highlighted in this survey include: 1) Lack of funds to support trichiasis surgery and related activities such as training of new trichiasis surgeons, refresher training for existing surgeons, follow up of patients and monitoring of surgical outcomes; 2) Shortage of trained human resources to manage post-operative trichiasis - in most trachoma endemic countries there are usually not enough trichiasis surgeons to clear the existing backlog of trichiasis cases and at the same time provide post-operative care and as a result, many people with post-operative trichiasis end up not receiving appropriate treatment; 3) Lack of proper follow-up systems for trichiasis patients after surgery which makes it difficult to monitor outcomes and provide post-operative care to the patients who need it; 4) Refusal by patients to undergo repeat surgery; and lastly, 5) Limited national data on the magnitude of trichiasis to inform planning, weak referral systems and limited number of secondary eye care units for post-operative care management.

To address the aforementioned challenges in the management post-operative trichiasis in Africa, the trachoma national programme coordinators who participated in this survey recommended a number of strategies. These strategies revolve around training, post-operative follow-up and care and monitoring of surgical outcomes.

Training of trichiasis surgeons

- Proper training of new TT surgeons using the HEAD START mannequin (International Coalition for Trachoma Control, 2018)
- Regular refresher training for existing surgeons to update their skills on new/improved surgical techniques
- Standardize post-operative TT management approaches and produce training manual for refresher training of trichiasis surgeons.
- Train more Ophthalmic Nurses to offer community-based eyelid surgery, which has been shown to produce comparable results to hospital-based surgery. This will help address the shortage of TT surgeons reported in most countries

Post-operative follow-up and care

- Strengthen the referral system to enhance patient follow-up and management of post-operative trichiasis
- Expand post-operative TT services at the primary eye care units by training of experienced TT surgeons or mid-level eye care workers to offer the services at this level. This will bring the

services closer to the communities thereby enhancing follow up and management of new and post-operative cases.

- Train and use community-health volunteers or community health workers to conduct home visits as a way of enhancing post-surgical follow up of patients.
- Proper infection control measures before, during and after surgery to reduce the risk of post-operative trichiasis and other poor outcomes.

Monitoring outcomes and surgical audits

- Systems and policies should be put in place to ensure structured monitoring of outcome and to audit surgeons' performance.
- Countries should use the ICTC preferred practices in conducting TT surgical campaigns and following up of patients after surgery.
- TT surgeons with an unacceptably high incidence of poor outcomes should be retrained and offered close and supportive supervision. If a surgeon fails to improve, he or she should be barred from performing surgery.
- Supportive supervision should be provided to new TT surgeons and those with a high incidence of poor outcomes to help reduce and manage poor outcomes.

DISCUSSION

WHO recommends that all national trachoma elimination programmes should strive to ensure that less than 10% of eyes have post operative trichiasis at one year post-surgery (World Health Organization, 2010). This survey indicates that over 52% of the trachoma-endemic countries have the same outcome targets (i.e. 90% good outcomes) as WHO. However, evidence from available literature suggests that these targets are rarely achieved; the incidence of post-operative trichiasis and others poor outcomes is reported to be much higher in many settings in Africa (West et al., 2005; Habtamu et al., 2017).

One of the possible reasons behind the huge discrepancy between the set targets and the actual outcomes achieved is the lack of policies and guidelines, systems and procedures to follow-up patients and monitor outcomes of trichiasis surgery. In this survey, only 14.8% countries reported having a national policy for follow-up of trichiasis patients after surgery, while an additional 27% of countries have adopted the adopted the ICTC preferred practice guidelines (International Coalition for Trachoma Control, 2015). These guidelines provide a framework for how to conduct an effective and efficient trichiasis surgical outreach program – from mobilizing patients to planning and organizing the outreach, surgical counselling, post-operative care, and recording and reporting program outputs. As most of the studies reporting incidence of post-operative trichiasis in Africa were conducted before the adoption and promotion of ICTC guidelines and other WHO manuals, it is possible that the

current and future incidence of post-operative trichiasis will be lower than that reported in studies published to date.

All except three countries recommend follow up at 3-6 months after surgery. In fact, most of the countries surveyed (59%) have at least three recommended follow up periods as part of their national policy or guidelines, matching WHO recommendation on follow up of patients after surgery. Due to the absence of national policies, systems and structures to follow-up patients after surgery, these recommendations have minimal or no link to actual practice. Consequently, in many countries, patients are lost immediately after surgery thereby exposing them to a renewed risk of blindness if they develop post-operative trichiasis. Further, without proper follow-up systems, regular monitoring of trichiasis surgery outcomes cannot be achieved.

Another contributing factor for the high incidence of post-operative trichiasis is the lack of policies for surgical audits of surgeons. According to WHO, surgical audits should be a part of ongoing supervisions within the national trachoma programme. The results of surgical audits should then be used to review the performance of trichiasis surgeons every 3 to 6 months after certification for new surgeons and (ideally) annually for existing surgeons, (World Health Organization, 2016). In line with this, national trachoma programmes are advised to consider setting up ongoing surgical audit procedures as part of their national strategies for maintaining surgical quality assurance (International Coalition for Trachoma Control, 2012).

Only 2 of the 27 trachoma endemic countries in Africa have a national policy to conduct surgical audits, however 63% of the countries surveyed reported some systems and procedures for audits of trichiasis surgeons. Furthermore, over two-thirds of the countries do not have a cut-off point at which poorly performing surgeons should discontinue surgery until retraining or other interventions have been undertaken. The implication of this is that, surgeons with an unacceptably high incidence of post-operative trichiasis and other poor outcomes continue to operate on patients thereby increasing the incidence of poor outcomes.

Despite the lack of national policies to guide surgical audits, 81% of the countries surveyed have either adopted other guidelines, such as those developed and promoted through the Queen Elizabeth Diamond Jubilee Trust, to inform their surgical audits or have put in place other supervisory systems and procedures. While this suggests that national programmes understand the need for surgical audits their implementation has been more limited.

CONCLUSION

The responsibility for managing post-operative trichiasis lies primarily with the national trachoma programmes. This responsibility is shared by individual surgeons, their supervisors, Ministries of health in the various countries, supporting partners, donors and WHO. Unfortunately, as evidenced in

this survey, most national trachoma programmes in Africa have set high targets for good outcomes, in line with WHO recommendations, but that these targets are rarely achieved due to lack of proper policies, systems and structures to support the targets. Further, most trichiasis patients are lost to follow up due to lack of proper systems to track the patients through the patient pathway, thereby making it difficult for the programmes to monitor the outcomes of trichiasis surgery and effect necessary interventions to manage post-operative trichiasis and other poor outcomes.

To address these challenges, it is recommended that, all national trachoma programmes in Africa should put in place proper monitoring systems and structures to follow-up patients, assess surgical outcomes and audit the performance of individual surgeons. In addition to monitoring the quality of trichiasis surgery, there is also a need to monitor indicators that reflect surgical output (i.e. the number of surgeries performed) and equity (such as the sex of patients receiving surgery and the geographical coverage of surgical services) as part of TT management. This involves collection of data on each operation performed for TT and outcome data for TT patients.

To enhance follow up of TT patients after surgery, a new tool (TT tracker) has been developed that aims to record and monitor outcomes and to conduct audits using smart phone technology. This tool has undergone pilot testing and will be rolling out in a selected countries in the coming months. It is envisaged that in future, all national trachoma programmes will adopt this tool as part of their monitoring system in an effort to improve outcomes of trichiasis surgery, which is critical to the global elimination of blinding trachoma.

Acknowledgements

The authors thank all the national trachoma programme coordinators who participated in this study.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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