Prevalence of increased intraocular pressure and presentation patterns of glaucoma
At a tertiary hospital in Malawi, South-East-Africa

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II List of Abbreviations

AAO    American Academy of Ophthalmology
ACA    Anterior chamber angle
ACD    Anterior chamber depth
ACG    Angle-closure glaucoma
AMD    Age-related macular degeneration
APD    Afferent pupillary defect
ASOCT  Anterior segment Optical Coherence Tomography
BE     Both eyes
BVA    Berufsverband der Augenärzte Deutschlands e.V.
B/VI   Blindness and vision impairment
CCT    Central corneal thickness
CDR    Cup-to-disc ratio
DALY   Disability-Adjusted Life Years
DOG    Deutsche Ophthalmologische Gesellschaft e.V.
GAT    Goldmann Applanation Tonometry
GON    Glaucomatous optic neuropathy
HM     Hand movement
IAPB   International Agency for the Prevention of Blindness
ICT    ICare Tonometry
IOL    Intraocular lens
ISGEO  International Society of Geographical and Epidemiological Ophthalmology
ISNT   Inferior-superior-nasal-temporal
IOP    Intraocular pressure
LSFEH  Lions Sight First Eye Hospital
MKW    Malawian Kwacha
mmHg   Millimetre of mercury
MSVI  Moderate and severe vision impairment
N    Sample number
ND   Normal distribution
NPL  No perception of light
NPV  Negative predictive value
NTG  Normal-tension glaucoma
OAG  Open-angle glaucoma
OCT  Optical Coherence Tomography
OPD  Outpatient Department
OR   Odds Ratio
ORA  Ocular-Response-Analyzer
PEX  Pseudoexfoliation syndrome
POAG Primary open-angle glaucoma
PPV  Positive predictive value
QECH Queen Elizabeth Central Hospital
RAAB Rapid Assessment of Avoidable Blindness
SSA  Sub-Saharan Africa
SD   Standard Deviation
SL-OCT Slit Lamp Optical Coherence Tomography
UK NSC United Kingdom National Screening Committee
US   United States of America
VCDR Vertical Cup-to-disc ratio
VI   Visual impairment
WGA  World Glaucoma Association
WHO  World Health Organization
1 Introduction: Blindness and Glaucoma with focus on developing countries

Loss of vision and blindness is an individual as well as a global health issue of major relevance. WHO estimated the global prevalence of blindness in 2010 with a world population of 6.7 billion. The number of visually impaired people is estimated to be 285.4 million (4.24%), 39.4 million (0.58%) of these are blind, and 246 million (3.65%) have low vision. (WHO 2010, 2014) Blindness seems to correspond to economic wealth of regions, as 90% of all blindness cases are found in developing countries, the largest numbers in the least developed countries, mostly Asia and Sub-Saharan Africa (SSA). (Resnikoff & Pararajasegaram 2001) (WHO 2012a) It was estimated that 1% of Africa’s population was blind in 2001. (Lewallen 2001)

In many regions of the world, glaucoma ranks second among blindness causing diseases. (Foster & Resnikoff 2005) As the development of glaucoma is related to age, this pathology is of major relevance especially in developing countries, because of the rising life expectancy which is currently seen in these countries. (Tham et al. 2014)

The following chapters are an introduction to blindness and glaucoma. Main facts and figures will be indicated with special focus on developing countries, especially Africa. The last part of the introduction will present objectives and aims of the present research.

1.1 Blindness

The following sections deal with blindness on a global scale, especially with numbers from Africa and Malawi. Furthermore, a definition of blindness is given as well as global causes of blindness, with differences between developing and developed countries. The term “avoidable blindness” is introduced. Positive trends and difficulties in the development of blindness prevalence are described.

1.1.1 Prevalence of blindness in Africa

SSA carries a great load of global blindness. While the population constitutes 12% of the global population, it accounts for 15% of the world’s visual impairment (VI). This
discrepancy is especially due to high numbers of ocular infectious diseases, e.g. trachoma and onchocerciasis, but also due to untreated cataracts. Often, preventable VI ranks as a major cause of disability in this part of the world. (Budenz et al. 2012) (Pascolini & Mariotti 2012)

There are regional differences occurring within the African continent, as B/VI in Naidoo’s survey was highest in West Africa and lowest in southern and central Africa. (Naidoo et al. 2014) A WHO data extrapolation indicates 1% of Malawians are blind, while 80% of those are supposed to be 50 years and older. A “Rapid Assessment of Avoidable Blindness” (RAAB) in Malawi from 2009/10 in the course of Vision 2020 planning calculated that 3.3% of people aged 50 and older are affected by blindness in southern Malawi. (Kalua et al. 2011)

Furthermore, an age above 50 and female gender are two factors associated with a higher risk of developing visual impairment. For example, 65% of those visually impaired and 82% of blind people are 50 years or above and it is predicted that by 2019, 84% of all people with VI will be 50 years or older. Speaking about gender differences globally, women form a larger part of B/VI. (Naidoo et al. 2014) (Resnikoff, S. et al. 2004) (WHO 2012a) (WHO 2013) This difference is most likely due to women’s longer life expectancy and lack of access to health services in many poorer societies. (Quigley & Broman 2006) (WHO 2007) In Africa, prevalence of moderate and severe vision impairment (MSVI) among men was 3.8%, but 4.2% for women. While 4.1% of men and 4.7% of women in West Africa had MSVI, in southern Africa the prevalence for men was only 2.0% and for women 2.3%. (Naidoo et al. 2014) Also in Malawi, age and female gender seem to be associated with blindness. People in the age group above 70 years as well as women seem to be more often affected by blindness. (Courtright 2003)

1.1.2 Definition of blindness

There are several definitions of blindness. The one used throughout this thesis is the definition used in abovementioned WHO data and most articles dealing with blindness. It is based on ICD-10, an internationally acknowledged health care classification system, maintained by WHO. It defines blindness as being present at vision of less than
3/60. In general, this classification of visual impairment comprises the following categories 0 to 5: (WHO 2015)

- Category 0 is mild or no visual impairment with vision of 6/18 or better.
- Categories 1 is MSVI with less than 6/18 and equal to or better than 6/60 (<6/18 to ≥6/60).
- Category 2 is MSVI with less than 6/60 and equal or better than 3/60 (<6/60 to ≥3/60).

Categories 1 and 2 are combined as “low vision”. Blindness is described in categories 3 to 5:

- Category 3 blindness is between 3/60 and 1/60 or finger counting at one meter (<3/18 to ≥1/60).
- Category 4 blindness ranges between less than 1/60 and light perception.
- Category 5 blindness has no light perception at all.

1.1.3 Causes of blindness

Various pathologies can be traced as underlying causes of blindness. As a major influencing parameter, ageing plays a role in the development of blindness. In the industrialised world, age-related macular degeneration (AMD) accounts for the largest proportion of blindness. On a global scale, though, about half of all blindness cases (51%) are caused by cataract, which is also mainly an age-related disease. Although there have been great improvements in the delivery of cataract surgery in developing countries, it is still the number one reason of blindness. In terms of VI in general, uncorrected refractive errors account for 42% of all cases and again cataract plays a major role, causing 33% of VI. (WHO 2010, 2012a) (Resnikoff, S. et al. 2004)

The second leading cause of blindness worldwide is glaucoma, with numbers indicated to cause between 8-12% of blindness. (Foster & Resnikoff 2005) (Pascolini & Mariotti 2012) (WHO 2010) In Cook’s study looking at the prevalence of blindness due to glaucoma in different African countries, glaucoma represents the second leading cause with up to 30%. (Cook 2009) In the RAAB for southern Malawi, including the district of Blantyre, in which the research of this thesis was conducted, glaucoma was also record-
ed as the second most common cause of blindness with 15.8%, after untreated cataract with 48.2%.

Another cause of blindness in Malawi is non-trachomatous corneal scarring with 12.3%. Trachoma has a rather low prevalence with 4.4% and onchocerciasis was not recorded at all. (Kalua et al. 2011) AMD comes third globally with 5%. In developed countries, though, it ranks first. Childhood blindness and corneal opacities cause 4% each, uncorrected refractive errors and trachoma 3% each, and diabetic retinopathy 1% of all blindness. Despite all research, 21% of blindness have undetermined causes. (WHO 2012a)

Numbers from 2010 regarding SSA depict a slightly different picture, in which glaucoma appears later in the list: cataract 35%, other or unidentified causes 33.1%, refractive error 13.2%, macular degeneration 6.3%, trachoma 5.2%, glaucoma 4.4%, and diabetic retinopathy 2.8%. (Naidoo et al. 2014)

It is worth mentioning, that most of abovementioned causes of blindness and visual impairment are treatable eye diseases. Hence, a large proportion of present blindness could have been or can be avoided with timely diagnose and treatment. Estimations by WHO state, that 75% of all blindness worldwide in 1996 could have been avoided, an assumption which gave rise to the term “avoidable blindness”. (WHO 2007) The WHO action plan 2014-2019 for universal eye health speaks of 80% of all causes of visual impairment which are preventable or curable. (WHO 2013) In accordance with this number, the RAAB in southern Malawi indicates that 75.4% of blindness is due to avoidable causes like glaucoma. (Kalua et al. 2011)

1.1.4 Decrease of blindness cases overall

A reduction of B/VI appears feasible knowing the fact that many causes are treatable and avoidable. In accordance with this hypothesis and despite previous figures about missed opportunities to save eyesight, there are positive trends in the development of global blindness, as explained in the following sections.

In response to the awareness of blindness as a health issue of worldwide impact, there have been international initiatives by WHO and associated partners such as the International Agency for the Prevention of Blindness (IAPB) to strive for a reduction or even
elimination of avoidable blindness. The “Global Initiative for the Elimination of Avoidable Blindness” from 1999 is also known as “VISION 2020: the Right to Sight”, with an action plan, revised in 2006 and 2013. It contains the joint aims of eliminating the main causes of avoidable blindness, and halting the doubling of the number of blind people by the year 2020, which is projected by researchers. On a national level they try to increase awareness and facilitate the implementation of eye health services. They have also tried to gain insight into causes of blindness and vision impairment (B/VI) in Africa. A major difficulty in realizing this attempt is the scarcity of epidemiological data, resulting in a call by WHO in 2004 for intensified research on eye disease prevalence in Africa. (Naidoo et al. 2014) (Resnikoff, S. et al. 2004) (IAPB 2010)

A comprehensive data set shows a worldwide decline of blindness prevalence over the last 20 years. International agencies see this as a success resulting from the fight against avoidable blindness, launched in VISION 2020. (IAPB 2013) In a WHO article comparing global data, a reduction of VI for example in the age group of 50 and older is seen, despite the rapid growth of this part of the population. The decline of VI in the elderly goes hand in hand with an improved socio-economic situation, as well as governmental and international efforts to contribute to eye health. (WHO 2012a)

Taking existing numbers from Africa, prevalence of B/VI has been substantially reduced between 1990 and 2010. Blindness (age-standardised prevalence) was reduced by 32% from 1.9% in 1990 to 1.3% in 2010 and MSVI decreased by 25% from 5.3% to 4.0% between 1990 and 2010. Statistically, absolute numbers of blindness and MSVI in Africa at all ages increased by 16% from 4.1 million blind in 1990 to 4.7 million in 2010 and 13 million with MSVI in 1990 to 16.6 million people in 2010. Nonetheless, there has been a general reduction of blindness prevalence due to the fact that the overall African population increased by 66% during the same time span. It is also a success regarding the fact that the African population is constantly ageing. (Bourne et al. 2013) (Naidoo et al. 2014)

Successful actions to achieve a reduction of blindness worldwide have been taken adamantly against blinding infectious diseases, such as trachoma, onchocerciasis, or against cataract with highly effective surgeries. In Malawi a reduction of blindness cases was
realized, most likely due to the increase of cataract surgeries from around 300 per million populations in 2003 to approximately 850 per million populations per year in 2010. (Kalua et al. 2011) Despite this positive trend of decreasing total blindness numbers, problem solution and prevention of blindness caused by glaucoma proves to be more challenging.

Different authors claim that tackling blindness from glaucoma is a bigger challenge in comparison to cataract for several reasons. The main reason is that cataract is easier to diagnose in comparison to glaucoma. The latter is not only asymptomatic at least in the first few years, but also more demanding in its detection, diagnosis, and treatment. Further, blindness caused by glaucoma is irreversible, as visual fields cannot be regained, whereas in cataract, surgery can usually reduce or even reverse visual impairment, which makes its treatment more effective. (Kingman 2004) (Kayange et al. 2014) Therefore, presentation patterns, treatment and impacts of glaucoma are important fields for research and public health if they want to contribute to the prevention of avoidable blindness caused by glaucoma, as shown in the next chapter.

1.2 Glaucoma

The following passages introduce the prevalence of glaucoma and blindness caused by the disease worldwide, with a focus on developing countries. The chapters elaborate on problems in the detection and awareness of glaucoma, general aspects like definitions, pathophysiology and risk factors. The two major types of glaucoma are introduced. These aspects are crucial for the study design, results and discussion of this thesis. Treatment, on the other hand, is not considered in the study and therefore not included in detailed elaborations. For theoretical basics on treatment see relevant scientific literature (e.g. (Kanski & Burk 1996) (Pfeiffer 2005) (Flammer 2001)).

The sections stress geographical variations in glaucoma prevalence. Despite decreasing numbers of blindness by chronic eye diseases, glaucoma is becoming an increasing burden to global and national economies and health systems. Therefore, one of the main questions of this thesis is the rationale for a glaucoma screening. This topic is dealt with in chapter 1.2.7.
1.2.1 Prevalence of glaucoma

The prevalence of glaucoma is part of the following section. There is divergent information about prevalence and because glaucoma is intimately associated with age, many prevalence indications are given in relation to it. On a worldwide scale, 1% of people older than 50 years are said to be affected by glaucoma, according to Adio and Onua 2012. (Adio & Onua 2012) Another pooled prevalence estimate by Tham et al is given for the population of 40 to 80 years in the year 2013, where the global prevalence of glaucoma in this age group is indicated as 3.54% (range 1.69-5.27). (Tham et al. 2014) Numbers are rising with higher age, which is particularly true for people of African descent. (Adio & Onua 2012)

Worldwide people are affected mainly by two major glaucoma types. 74% of patients globally suffer from primary open-angle-glaucoma (POAG) and 26% from angle-closure glaucoma (ACG). According to Quigley and Broman this corresponds to a global prevalence of 1.96% in POAG as well as 0.69% of ACG in 2010, giving 2.65% combined. While 80% of ACG patients are Asians, POAG is most prevalent in Africa and among people with African descent. (Quigley & Broman 2006) (Lawan 2013) Tham et al give differing numbers and indicate that worldwide glaucoma (POAG and ACG combined) prevalence is 3.54%, as mentioned above, of which ACG makes 0.5% and POAG makes 3.05%. (Tham et al. 2014) Conclusively, there is a range of 1% to 3.54% global glaucoma prevalence in the cited literature. Differences might result from varying glaucoma definitions, criteria and age ranges among other reasons.

It is estimated that in Africa the prevalence of glaucoma in people of 40 years and older is about 4%, (Cook 2009) but numbers vary in different regions and ethnic groups and also in between literature, but are especially high in West Africa, as shown in Table 1 below.

Tham’s literature review stresses the geographical variations regarding glaucoma. Comparing different world regions, glaucoma prevalence ranked highest on the African continent with 4.79% (range 2.63-8.03). Thereof POAG makes 4.2% (range 2.08-7.35) and ACG 0.6% prevalence. (Tham et al. 2014) In Ghana, POAG affected 8.5% of people aged 40 years and older in 2010, up to 13 to 18% in people older than 64 years, but
also 7.7% in patients between 30 and 40 years of age. (Ntim-Amponsah et al. 2004) These numbers rank among the highest in the world. (Gyasi et al. 2010) Budenz states that preventable vision loss from glaucoma is a major problem in the Ghanaian population. (Budenz et al. 2012)

Table 1 outlines the geographical variance within Africa and gives examples of glaucoma prevalence and/or types in South Africa, Tanzania, and Ghana.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of publication</td>
<td>1993</td>
<td>2003</td>
<td>2000</td>
<td>2004</td>
</tr>
<tr>
<td>Country</td>
<td>South Africa (Western Cape)</td>
<td>South Africa (North-West)</td>
<td>Tanzania</td>
<td>Ghana (West Africa)</td>
</tr>
<tr>
<td>Number of participants</td>
<td>987</td>
<td>839</td>
<td>3268</td>
<td>1785</td>
</tr>
<tr>
<td>Age group</td>
<td>40 years or older</td>
<td>40 years or older</td>
<td>40 years or older</td>
<td>40 years or older</td>
</tr>
<tr>
<td>All Glaucoma prevalence</td>
<td>-</td>
<td>5.3</td>
<td>4.16</td>
<td>-</td>
</tr>
<tr>
<td>Primary open angle glaucoma prevalence</td>
<td>1.5</td>
<td>2.9</td>
<td>3.1</td>
<td>8.5</td>
</tr>
<tr>
<td>Primary closed angle glaucoma prevalence</td>
<td>2.3</td>
<td>0.5</td>
<td>0.59</td>
<td>-</td>
</tr>
<tr>
<td>Secondary glaucoma prevalence</td>
<td>-</td>
<td>2.0</td>
<td>0.47</td>
<td>-</td>
</tr>
</tbody>
</table>

Glaucoma prevalence is rising, but nevertheless the first phase of VISION 2020 starting in 1999 did not focus on glaucoma yet. It was therefore not listed among the top five eye diseases, which were cataract, trachoma, onchocerciasis, childhood blindness, and uncorrected refractive errors – diseases with easier and more effective and promising
treatment options. (Babalola 2011) WHO claims that most glaucoma forms can be managed successfully and it is therefore advisable to consider it in national VISION 2020 programmes. In the meantime, as shown in the next passage, glaucoma is now one of WHO’s focus points in VISION 2020 and also on WHO’s list of priority eye diseases. (WHO 2015b) (WHO 2015a)

Rising numbers of glaucoma support the importance of tackling the issue in international and national health programmes. In 2010, more than 60 million people (aged 40-80) were expected to suffer from glaucoma worldwide. 60.5 million affected people in 2010 were projected by Quigley and Broman in 2006 and 64.3 million according to Tham et al. (Quigley & Broman 2006) (Tham et al. 2014) Calculations show that glaucoma will increase to about 80 million in 2020. (Quigley & Broman 2006) A systematic review and meta-analysis projects a rise of people affected by glaucoma to 111.8 million by 2040, a 74% increase compared to 64.3 million in 2013. (Tham et al. 2014)

Most ponderous are increasing numbers in Africa and Asia, whereof Asia will shelter the largest number of POAG and ACG. Africa’s number of glaucoma cases will increase by 130.8% (10.9 million) from 2013 to 2040, developing from 8.29 million in 2013 to 10.31 million in 2020 to 19.14 million people with glaucoma in 2040. In Europe, northern America and Oceania there will only be a minor growth in numbers. (Tham et al. 2014)

This upsurge in glaucoma cases can mostly be explained by ageing populations all over the world. Increasing life expectancy will be most strikingly in Africa and Asia, while in the western world age structures are rather stable. (Tham et al. 2014) (Budenz et al. 2012) Tham et al. found that people living in urban areas were 58% more likely to present with POAG than people in rural areas. Possible explanations in the article are the higher incidence of myopia among urban populations and a difference in lifestyle, regarding stress, pollution, physical activity or diet. (Tham et al. 2014)

Glaucoma is not only important in terms of prevalence, but because of the detrimental effects of vision loss on an individual’s personal and professional life and consecutively on a country’s economy.
1.2.2 Blindness from glaucoma

Approximately 8% of all blindness is due to glaucoma, the second leading cause worldwide, as mentioned in [1]. (Pascolini & Mariotti 2012) (WHO 2010) Quigley and Broman compare several surveys and find differing numbers. Previous studies gave a number of 4.4 million (12%) of blindness caused by glaucoma, while another suggests 8.4 million (>20%) bilaterally blind from glaucoma in 2010 and 11.1 million in 2020. The reason for this discrepancy, as Quigley and Broman explain, is a difference in methodology of prevalence surveys. Many underestimate glaucoma numbers by focusing more on “treatable” diseases as causes of blindness, such as cataract. (Quigley & Broman 2006) Adio and Onua claim glaucoma to cause as much as one third of current blindness. (Adio & Onua 2012)

The risk of blindness resulting from glaucoma varies among individuals, ethnic groups, and regions, but it is particularly high in patients from developing countries. (Chen 2004) (Quigley 1996) (Ramchandani 2006) In SSA glaucoma caused 4.4% of blindness in 2010, according to Naidoo et al., while Resnikoff et al. speak of 15%. (Naidoo et al. 2014) (Resnikoff, S. et al. 2004)

Table 2 demonstrates the percentages of blindness due to the main causes, namely glaucoma, as well as cataract, trachoma, and macular degeneration in different African regions and Africa in total compared to global data.
Table 2: Blindness in Africa and worldwide by causes (modified after Naidoo et al. 2014)

<table>
<thead>
<tr>
<th>Region</th>
<th>Glaucoma Blind (%)</th>
<th>Cataract Blind (%)</th>
<th>Macular degeneration Blind (%)</th>
<th>Trachoma Blind (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1990</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central Africa</td>
<td>3.3</td>
<td>41.0</td>
<td>4.8</td>
<td>0.94</td>
</tr>
<tr>
<td>East Africa</td>
<td>2.9</td>
<td>35.4</td>
<td>4.1</td>
<td>13.5</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>5.4</td>
<td>34.0</td>
<td>6.9</td>
<td>1.6</td>
</tr>
<tr>
<td>West Africa</td>
<td>2.9</td>
<td>37.1</td>
<td>4.1</td>
<td>7.3</td>
</tr>
<tr>
<td>Africa</td>
<td>3.1</td>
<td>36.5</td>
<td>3.8</td>
<td>8.9</td>
</tr>
<tr>
<td>World</td>
<td>4.4</td>
<td>38.6</td>
<td>4.9</td>
<td>2.8</td>
</tr>
<tr>
<td><strong>2010</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central Africa</td>
<td>5.2</td>
<td>34.8</td>
<td>6.9</td>
<td>0.44</td>
</tr>
<tr>
<td>East Africa</td>
<td>4.0</td>
<td>36.7</td>
<td>5.8</td>
<td>8.1</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>7.3</td>
<td>31.2</td>
<td>9.7</td>
<td>0.69</td>
</tr>
<tr>
<td>West Africa</td>
<td>4.4</td>
<td>33.8</td>
<td>6.2</td>
<td>3.6</td>
</tr>
<tr>
<td>Africa</td>
<td>4.4</td>
<td>35.0</td>
<td>6.3</td>
<td>5.2</td>
</tr>
<tr>
<td>World</td>
<td>6.6</td>
<td>33.4</td>
<td>6.6</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Also Table 3 shows that regional differences of blindness owing to glaucoma within Africa are tremendous. Interregional discrepancies are large among all cited authors, with over 30% in a Nigerian study compared to 6% in a South African research. In many studies though, as already mentioned above, glaucoma ranks second among all causes of blindness. The regional variance proves the importance of research within the different parts of the world for better and more targeted health programmes. The strong differences especially regarding blindness levels might be partially due to the large time difference. Registration of blindness cases in the late 1980s and 1990s might not have reached all parts of the population.
Table 3: Prevalence of Blindness, Proportion owing to Glaucoma, Ranking (modified after Cook 2009)

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Country</th>
<th>Surveyed Ages</th>
<th>Overall Blindness Prevalence, %</th>
<th>Proportion of Blindness Owing to Glaucoma (%)</th>
<th>Ranking of Blindness Owing to Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bucher</td>
<td>1988</td>
<td>South Africa</td>
<td>All ages</td>
<td>0.57</td>
<td>6.0</td>
<td>Fourth</td>
</tr>
<tr>
<td>Balo</td>
<td>1989</td>
<td>Togo</td>
<td>All ages</td>
<td>0.82</td>
<td>6.0</td>
<td>Second</td>
</tr>
<tr>
<td>Negrel</td>
<td>1990</td>
<td>Congo</td>
<td>All ages</td>
<td>0.30</td>
<td>9.0</td>
<td>Second</td>
</tr>
<tr>
<td>Cook</td>
<td>1993</td>
<td>South Africa</td>
<td>All ages</td>
<td>1.00</td>
<td>22.9</td>
<td>Second</td>
</tr>
<tr>
<td>Negrel</td>
<td>1995</td>
<td>Benin</td>
<td>All ages</td>
<td>0.6</td>
<td>15.0</td>
<td>Second</td>
</tr>
<tr>
<td>Melese</td>
<td>2003</td>
<td>Ethiopia</td>
<td>40 years and older</td>
<td>7.9</td>
<td>7.6</td>
<td>Third</td>
</tr>
<tr>
<td>Guzek</td>
<td>2005</td>
<td>Ghana</td>
<td>40 years and older</td>
<td>4.4</td>
<td>20.6</td>
<td>Second</td>
</tr>
<tr>
<td>Adegbibe-</td>
<td>2006</td>
<td>Nigeria</td>
<td>60 years and older</td>
<td>5.6</td>
<td>32.4</td>
<td>Second</td>
</tr>
<tr>
<td>Onakpoya</td>
<td>2007</td>
<td>Nigeria</td>
<td>All ages</td>
<td>1.1</td>
<td>14.3</td>
<td>Second</td>
</tr>
</tbody>
</table>

The high risk of going blind from glaucoma in developing countries has multiple origins. Firstly, the awareness among affected individuals is low. Therefore, individuals present late to specialists, often already blind in at least one eye upon first presentation. Secondly, infrequency of ophthalmologic check-ups leads to advanced stages. (Ntim-Amponsah et al. 2005) Thirdly, among Africans the disease is more aggressive and leads to earlier blindness. (Kyari et al. 2013) And lastly, the number of ophthalmologists in developing countries is very low in comparison to more developed, industrialised countries, which reduces the chance of regular medical examinations. (Gyasi et al. 2010) Further reasons for the high risk of becoming blind from glaucoma especially in Africa will be discussed in chapter 1.2.6.

As discussed in the previous chapter, glaucoma was not put on the VISION 2020 priority list of eye diseases, which was mainly due to uncertainty or inability to detect and manage this pathology. (Cook 2009) Nevertheless, recent efforts show that tackling the problem of this blinding disease gained importance internationally and in Africa. In
2010 Ghana hosted the World Glaucoma Association’s (WGA) first Africa glaucoma summit. Its participants stressed to improve glaucoma management, training, and education, and include them into existing national programmes. In 2012, the Kampala Resolution constituted another reminder for those in glaucoma care to raise awareness of the disease and incorporate it into eye care services and policies. (WGA 2010) (PBU 2012)

Despite the blinding effect of glaucoma, which arises typically late in the progress of the disease, the lack of symptoms and knowledge often leads to unawareness among affected people, as discussed in the following section.

1.2.3 Detection and awareness

Globally only a limited proportion of glaucoma patients are diagnosed or treated. Prevalence surveys suggest that in the developed world, about half of all cases are likely to be diagnosed. However, in developing countries, especially in very remote and medically underserved parts, the number of detection is probably closer to one in ten or less. (Ntim-Amponsah et al. 2004) (Rotchford 2005)

Glaucoma is sometimes called the “thief of sight”. This name stems from the asymptomatic progression and nature of the disease, which leads to patients being unaware of their potentially blinding disease and doctors having difficulties detecting it. (Faal 2012)

Kyari et al. underline the low awareness of glaucoma by scrutinizing several articles comparing awareness, attitudes, and knowledge of glaucoma patients in different African settings. (Kyari et al. 2013)

The high rate of undiagnosed glaucoma may further be due to the complex diagnosis and poor availability of adequate eye care facilities, staff, and equipment. (Olawoye et al. 2013) Mermoud, a Swiss ophthalmologist and founder of the charity “Vision for all”, names the lack of well-trained eye doctors to be the main limiting factor in diagnosing and managing glaucoma patients in the developing world. He continues to elaborate on the disproportion between doctors and patients. Whereas in Europe one ophthalmologist serves 10 000 patients, in India there is one eye doctor for 400 000, while in Africa it is one or even less for a million patients. (Kingman 2004)
Nevertheless, diagnostic technology and thus detection are improving, which might in part explain the increasing numbers of glaucoma prevalence. (Cedrone et al. 2008) This is true for settings of industrialised environments, and may also be applicable for developing countries. The next chapter introduces possible definitions, classifications, pathophysiology, and diagnostics of glaucoma. It highlights special features of the African setting and creates a base for the following presentation and discussion of results.

### 1.2.4 Definition and classifications

There has not yet been an international definition of glaucoma. (Pfeiffer 2010) This uncertainty makes diagnosis and comparison of various epidemiological studies difficult, because they often use different definitions which can lead to considerably varying numbers and outcomes. (Weinreb et al. 2008)

It is crucial to stress that glaucoma in general is now considered a group of diseases, not one disease alone. Therefore, Pfeiffer speaks of glaucoma in plural (German: Glaukome). (Pfeiffer 2005) In a review of studies on how to define chronic open-angle glaucoma (OAG), the authors found different combinations of mainly three parameters “glaucomatous optic nerve appearance”, “visual field defect” and “elevated intraocular pressure (IOP)”. These three features played a major role in most studies. (Spry & Sparrow 2005) The following paragraphs are a brief summary of three existing glaucoma definitions.

One example is the definition by the UK National Screening Committee (UK NSC), defining glaucoma as “a chronic, age-related optic neuropathy characterised by at least one eye having a defined visual field abnormality combined with an optic disc appearance compatible with the functional loss.” (Spry & Sparrow 2005)

In 1998, the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) suggested a standard definition and classification system for glaucoma, which takes different diagnostic possibilities into consideration. This seems a practical approach given the fact that firstly, not all examinations are possible in each patient and secondly, not all tools may be present at different settings, e.g. in many developing countries. ISGEO defines glaucoma as structural optic nerve damage with functional deficit. Three levels of evidence describe the disease, without considering angle fea-
tures. The highest level presents the assessment of structural damage in terms of a large vertical cup-to-disc ratio (VCDR), ≥97.5th percentile of the VCDR of the normal population and functional damage in terms of visual field defects. Level two has stronger optic disc damage >99.5th percentile, or asymmetry, if visual field testing is unavailable. Level three, if cup-to-disc ratio (CDR) and visual fields cannot be assessed, IOP >99.5th percentile of the normal population, visual acuity (VA) less than 3/60 and medical history of glaucoma could help in defining glaucoma. (Kyari et al. 2013) (Foster et al. 2002)

A further category is glaucoma suspect. These individuals either have glaucoma suspicious optic discs with IOPs below 22 millimetre of mercury (mmHg) with an unsuspicious visual field, or borderline optic discs with IOPs above 21 mmHg, or further risk factors or borderline optic discs with non-accessible or non-utilisable visual fields. (BVA & DOG 2006)

A concluding remark regarding definitions by Kyari et al. relativises the theoretical discussion and puts focus on the practical consequences. He claims that although surveys vary in definitions and methodologies and are thus not totally comparable, the main conclusion is “that glaucoma is a public health problem in SSA”, (Kyari et al. 2013) and therefore the topic needs further consideration and research.

In summary, after introducing different definitions and classifications, it can be defined as usually bilateral, often asymmetric disease, which shows the following features in at least one eye: glaucomatous optic nerve damage, glaucomatous visual field defect, repeatedly IOPs above 21 mmHg, a disease onset during adulthood and absence of any secondary reasons for glaucoma. Nevertheless, 15% of all POAG patients constantly present with IOPs below 21 mmHg and thus are diagnosed with so called normal tension glaucoma (NTG). (Kanski & Burk 1996)
1.2.5 Pathophysiology and diagnostics

Glaucoma, as defined above, is not one disease but a set of pathologies with some common and some varying pathologic and diagnostic features, explained at length in respective text books. A few special aspects arise in the African context and are explained below.

In glaucoma, a still incompletely understood underlying pathologic process is silently and gradually destroying retinal nerve fibres of the optic nerve. This results in nerve fibre loss, which first strikes the optic nerve head. (Flammer 2001) A large quantity of nerve fibres may already be destroyed before a patient consciously perceives visual impairment in the form of a reduced visual field. Twenty percent ganglion cell loss corresponds to five decibel sensitivity loss and ten decibel sensitivity reduction with already 40% ganglion cell loss. (Quigley et al. 1989)

CDR is genetically determined and in most eyes it is 0.3 or below. Ratios above 0.3 in one eye, or a difference in the ratios of more than 0.1 between both eyes should be regarded as suspicious. (Kanski & Burk 1996) For diagnostics among an African population it has to be mentioned, that these often present with larger optic discs. This has to be respected in CDR assessments. (Nangia et al. 2013)

The origins and risk factors of the abovementioned nerve fibre loss will be discussed in more detail in section 1.2.6. One relevant factor, though, is IOP. Normal values range between 10 and 21 mmHg (average 16 mmHg) and fluctuate within a 4 mmHg-range in healthy eyes, depending upon daytime, blood pressure and other factors. Glaucomatous eyes may even vary within a 10 mmHg-range. In general terms, IOP is now considered to be normal if it does not harm the eye and is thus individually determined. (Kanski & Burk 1996)

For diagnostics of glaucoma, all these pathologic features should be assessed. It is further important to assess the optic nerve head by funduscopy through a dilated pupil. Findings should be documented by drawing or photograph for better comparison during follow-up and judgment of progression. As a final examination, visual field should be assessed by perimetry. (Kanski & Burk 1996) In African settings visual field tests are often “unavailable and unnecessary”, as Bowman and Kirupananthan write in their
article on “How to manage a patient with glaucoma in Africa”. (Bowman & Kirupananthan 2006) This lack of visual field diagnostics in developing countries may result in an underestimation of glaucoma prevalence. One alternative which can be useful in developing countries is funduscopy with optic disc assessment in combination with a drawing of the fundus. This method is subjective and far from ideal, but it allows getting an approximate prevalence of glaucoma, detecting advanced disease stages and giving at least some (drawn) documentation for a better follow-up. (Foster et al. 2002)

1.2.6 Risk factors

In the African context of the current study an accumulation of several individual risk factors for the development of glaucoma is found. This phenomenon may in part be an explanation for the importance and high prevalence of this pathology.

The AAO has published guidelines on Preferred Practice Patterns® for POAG. This paper itemises the following risk factors associated with POAG: (AAO 2010b)

- Increased intraocular pressure
- Old age
- Family history of glaucoma
- African ancestry or Latino/Hispanic ethnicity
- Thin central cornea thickness
- Low ocular perfusion pressures
- Type II diabetes mellitus
- Myopia
- Genetic mutations

Flammer distinguishes between risk factors for increased IOP values (e.g. age, familial predisposition, race, arteriosclerosis, and myopia), from risk factors for glaucomatous damage. The latter are increased IOP, vascular dysregulation with arterial hypotension and vasospasm, female gender, and race. (Flammer 2001) Risk factors which are of importance in the setting of this thesis will be elucidated in more detail in the following paragraphs.
**Increased intraocular pressure levels** are a well-known and widely discussed potential and potent risk factor in the development of glaucomatous damage. The higher the pressure, the greater is the likelihood to develop optic nerve damage. Variation of pressure with spikes may even be more harmful to the optic nerve than high pressure alone, and patients with undulating IOPs are more likely to have severe glaucoma progression. The duration of elevated pressure is crucial. An acute rise, as e.g. during a glaucoma attack, does not necessarily cause harm if the IOP is lowered promptly, in comparison to a detrimental chronic elevation.

Stewart stresses the relevance of increased IOP for glaucoma damage and the progression of disease especially in eyes with mean IOP higher than 21 mmHg. (Stewart *et al.* 1993) (Stewart *et al.* 2000) The Ocular Hypertension Treatment Study (OHTS) mentions that lowering IOP leads to a significant reduction of disease progression. (OHTS & EGPS 2007) If this opportunity is missed, as in many cases in the developing world, a chance to avoid optic nerve damage is lost. Leske et al. found in follow-ups on treated and untreated POAG patients that initial IOP reduction was most important regarding the outcome, since every lower or higher mmHg in IOP occurred with approximately 10% decrease or increase in the risk for progression of visual field defects. (Leske *et al.* 2003) Spry and Sparrow also found that the higher the IOP, the higher the risk of progression of the disease to end-stage nerve damage. (Spry & Sparrow 2005)

Nevertheless, 30% of people have glauomatous nerve damage without detectable IOP elevation, whereas almost 80% of patients with increased IOP levels never progress on to glaucomatous damage. (Flammer 2001) Therefore, IOP is a potential but not necessary risk factor for the development of glaucomatous damage to the optic nerve.

**Ageing** plays an important role in glaucoma for several reasons. Firstly, with lifetime ageing processes occur in the trabecular meshwork, and IOP average will increase. Secondly, because life expectancy rises worldwide, age-related diseases occur more frequently. Thereby, the development of increased IOPs and further glaucoma with age can be expected to pose an increasing burden on eye care services throughout the African continent and elsewhere. The majority of patients with increased IOP and POAG are above 40 years and do not only show the physiologically occurring rise of IOP with
age, but a more severe increase of pressure. The reasons might be genetic, but are not yet fully understood. In most glaucoma patients, IOP starts to rise between the ages of 40 to 50. If no treatment is initiated at this stage, which is often the case in developing countries, the pressure is likely to rise further. Thirdly, the lifetime of elderly patients leads to an accumulation of nerve fibre damage. Therefore, visual field defects commonly become apparent with age even without an elevated IOP. (Flammer 2001) (Kingman 2004)

**Familial predisposition** can be responsible for increased IOP and progression of glaucoma. The tolerance of an eye for high IOP levels and the individual limit is only incompletely understood. The risk for glaucomatous damage in individuals with affected family members is comparably high and those patients should be monitored carefully. (Flammer 2001) (Tielsch et al. 1994) In developing countries, though, family history of a disease is often unknown and patients are unaware of it. Thus, such factors are often difficult to assess and hard to act accordingly.

In line with hereditary factors, **race or African ancestry** are named among major risk factors for high IOP, as well as glaucoma development. Epidemiological studies illustrate a dramatic increase of glaucoma with age, especially among patients of Hispanic and African descent. (AAO 2010b)

This reinforces the statement of innate risk factors being present in the sample population of the present study, as geographical, ethnic, or genetic origins put them at higher risk for developing glaucoma. Flammer portends it is often difficult to fully distinguish between hereditary and socioeconomic reasons or living conditions. Nevertheless, in Africans, high IOP occurs more frequently and at an earlier age and also the chance of developing optic nerve damage at a given IOP is higher. (Flammer 2001)

Other authors support the finding that between Caucasians and Africans, there is a different dynamic in glaucoma development. In Africans glaucoma tends to occur at an earlier age. Further, it is often associated with higher IOP, it may be more rapidly progressive and patients present later in the course of their disease, with up to 50% of patients already blind in one eye at the point of first presentation. (Cook et al. 2009)
This fact was first recognized in the US by examining the American population, finding differences between white Americans and Afro-Americans. A study states that prevalence rates for POAG in black people were four to five times higher than in whites. (Tielsch et al. 1994; Tielsch 1991)

Another innate glaucoma risk factor is gender. Studies report opposing gender differences. (Tham et al. 2014) (Quigley & Broman 2006) (Adio & Onua 2012) A US-study found no difference in rates of POAG between men and women for either blacks or whites. (Tielsch 1991) (Cedrone et al. 2008) Whereas no difference is found in IOP levels between both sexes, the following study described differences in the prevalence of the individual types of glaucoma. In general, more women than men were said to be presently and prospectively affected by glaucoma. For 2010 it was estimated that females would comprise 55% of POAG, 70% of ACG, and 59% of all glaucoma. Respectively, women were more likely to fall ill with ACG and NTG, while men more often presented with pigment dispersion glaucoma. (Quigley & Broman 2006) Furthermore, women seemed to be extremely sensitive to higher pressures, as they commonly developed glaucomatous damage if affected with POAG. A reason for the higher incidence of NTG in women might be the higher incidence of vasospastic disorders in females. (Flammer 2001) Conclusively, no clear gender bias can be seen.

Central corneal thickness (CCT) is a considerable parameter and relevant part of glaucoma discussions, especially as it is considered to be an independent risk factor for glaucoma development. (AAO 2010b) (Boehm 2011) Corneal thickness varies among individuals, among ethnic groups, and differs within ophthalmologic pathologies.

Depending on the measurement technique, the human eye possesses an average CCT of 540 µm. Doughty and Zaman recommend that if a +/- 1 standard deviation (SD) estimate of acceptable population variance is used, CCT values between 503 and 565 µm in adult eyes should be considered normal, from a clinical and also a clinical research perspective. (Doughty & Zaman 2000) (Rosentreter 2011) Another comparable average is given with 550 µm. The average of patients with POAG was reported to be 545 µm,
in NTG it is about 510 μm and those with ocular hypertension about 595 μm. (Neuburger et al. 2011)

Furthermore, a relevant fact for the present study sample is that Africans as well as Afro-Americans, in comparison to Caucasians or other ethnic groups, are known to have thinner corneas with approximately 534 μm average. (Lawan 2013) (Leite et al. 2010) (Aghaian et al. 2004) In the current study population of Malawi, Hohmann detected one of the lowest CCT-measurements among all available study data on people of African descent with an average in a non-glaucomatous sample of 509.83 μm. (Hohmann 2011) This feature will also be part of the discussion.

To summarize, the study sample consisting of people from Malawi in South-East-Africa comprises several innate risk factors. Based on the African origin, which can be associated with higher IOP and thus a predisposition to develop glaucoma early and aggressively, the population also seems to be prone to thin CCTs, another crucial risk factor in the development of glaucoma. Thus, the special preconditions and pre-existing risk factors in this population make glaucoma research a crucial scientific and medical undertaking in this setting.

1.2.7 Rationale for glaucoma screening

The biggest challenge, as well as opportunity in blindness caused by glaucoma is inherent in the fact that this irreversible blindness can be prevented or delayed through timely diagnosis, effective treatment, and regular clinical follow-ups. A logical conclusion is trying to detect the disease as early as possible before irreversible damage has occurred. One such method is screening.

Screening was defined in 1951 by the United States Commission of Chronic Illness as “the presumptive identification of unrecognised disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly. Screening tests ought to sort out persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment.” (Commission on Chronic Illness 1957)
Spry and Sparrow evaluate POAG as a major cause of visual loss, which consequentially deserves consideration for screening despite the need to possibly use more than one test. Their elaboration refers back to the 22 criteria of the United Kingdom National Screening Committee (UK NSC), which are a framework regarding condition, test, treatment, and screening for glaucoma. (Spry & Sparrow 2005) (UK NSC 2015) The UK NSC criteria are a variant of the classic WHO screening criteria published in 1968 by Wilson and Jungner, known as “Wilson criteria”: (Wilson & Jungner 1968)

1. The condition sought should be an important health problem
2. There should be an accepted treatment for patients with recognized disease
3. Facilities for diagnosis and treatment should be available
4. There should be a recognizable latent or early symptomatic stage
5. There should be a suitable test or examination
6. The test should be acceptable to the population
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood
8. There should be an agreed policy on whom to treat as patients
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
10. Case-finding should be a continuing process and not a “once and for all” project

Spry and Sparrow come to the conclusion that in case of POAG the criteria are largely even, though not completely met. (Spry & Sparrow 2005) German ophthalmic experts (“Berufsverband der Augenärzte Deutschlands e.V.” (BVA) and „Deutsche Ophthalmologische Gesellschaft e.V“ (DOG)) conclude that in case of POAG the main criteria for screening are fulfilled. However, according to Lawan, the nature of the disease (point 7) cannot be regarded as fully understood. (Lawan 2013)
As elaborated in chapter 1.2.1 and 1.2.2, glaucoma can be considered a problem of global and national public health especially in regions with increasing life expectancy (point 1). Risk factors and treatment options for the disease are known to a large extent. Tests for diagnostics and monitoring are available. Therefore, points 1 to 4 are met, but point 5 is not fully agreed on.

A prevailing challenge in diagnosing glaucoma is to identify a test with which to reliably diagnose glaucoma in its early stage and could thus be used for screening. Three tests - tonometry, optic disc/nerve fibre layer examination and visual field testing - are essentially used in the diagnosis of POAG. They have also been considered potential and well-accepted screening tools. (Spry & Sparrow 2005) According to Rotchford and the present state of knowledge, none of these have high enough levels of sensitivity and specificity, so that a large number of false positives are referred. (Rotchford 2005) (Mowatt et al. 2008) (Lawan 2013)

Hohmann suggests that in a setting like Africa, in which the number of unidentified glaucoma cases is even higher than in other parts of the world, with low density in eye clinicians, difficult work conditions, and a low degree of health education, a simple screening method such as the mobile ICare tonometer (ICT) device would provide substantive benefit. Further, IOP measurements were recommended as a screening method in developing countries, since it is one of the few simple options at present to detect (advanced) glaucomatous eyes among a healthy population. According to Hohmann, it enables to filter out patients with very high IOP values and some remaining vision. These can then be transferred to larger hospitals for further examination. (Hohmann 2011) Although this seems a realistic practicable action, the inevitable controversy in this suggestion is the fact that a great amount of glaucoma cases will be missed by tonometry alone as they present with IOPs in the normal range. (Cook 2009)

The right tool, timing and target group are challenges for screening. Regarding glaucoma in low-income countries, WHO in the action plan on the prevention of visual impairment advices that opportunities for diagnosing glaucoma should be identified, e.g. during refraction testing, or before/after cataract surgery. (WHO 2007) Essuman and
Ntim-Amponsah recommend using every opportunity that presents itself for diagnosing glaucoma cases. (Essuman & Ntim-Amponsah 2012)

Transferred to a setting with populations at risk like Africa, a comprehensive eye evaluation including glaucoma assessment, e.g. during community eye outreach programmes, offer a realistic chance for earlier diagnosis. (Cook 2009) A Nigerian study concluded that community eye outreach programmes appeared highly useful in the earlier detection of glaucoma in SSA. It is often during routine ocular examinations that diseases without early symptoms, like glaucoma, are detected. (Olawoye et al. 2013) Presently in the United Kingdom, glaucoma is also usually detected opportunistically by optometric case finding. (Spry & Sparrow 2005)

Nevertheless, with the current state of knowledge and diagnostic tools, a general glaucoma screening of a whole population for early detection is not cost-effective and not used anywhere in the world. In the future, though, if technologies for glaucoma screening advance, population-based screening might become a beneficial procedure. At present, if screening programs target populations at risk, namely people of old age, with a genetic predisposition or certain heritage, e.g. African Americans or Hispanics, it can be considered a useful and cost-effective tool. (AAO 2010b) The AAO suggests, especially among older populations, that screening for glaucoma during general eye disease screenings could be pursued. (AAO 2010b)

One of the major questions of this thesis, as will be outlined in the next chapter, are about the rationale of screening, as well as possible screening options and guidelines in the population under study, which are elaborated in chapter 4.5 and 4.6 according to results presented in this thesis. Possible age and IOP cut-offs will be discussed in chapter 4.5.2 and 4.6, as currently there are no universal guidelines in this respect. (Spry & Sparrow 2005)
1.3 Research objectives and aims

After dealing with the main terms and issues important for the study, general research objectives will be formulated. These objectives are in accordance with abovementioned questions and challenges, which make research in this field a crucial undertaking.

A major aim of this research was to document baseline parameters of healthy and glaucomatous eyes in a geographic region in which data is scarce. Specific aims were to investigate the prevalence of raised IOPs above 21 mmHg, and especially the prevalence of glaucoma with subtypes, and associated risk factors among patients presenting at Lions Sight First Eye Hospital (LSFEH) in Blantyre, Malawi. This aim is consonantly with the call by WHO in 2004 for intensified research on eye disease prevalence in Africa, due to the scarcity of epidemiological data, also stated by other literature. (Naidoo et al. 2014) (Resnikoff, S. et al. 2004) (IAPB 2010)

The study aims at creating a database for the respective geographical region with information regarding features of healthy and glaucomatous eyes, with a focus on IOP, optic disc appearance and corneal thickness. It aids at understanding and knowing characteristic presentation patterns of glaucoma, enabling more effective detection, and management of glaucoma in this region. As IOP in normal eyes varies not only inter- and intra-individually but also between populations, data analysis, as well as any screening test based on tonometry, has to take the specific IOP levels in a particular population into account. (Rotchford 2005) It is therefore important to create baseline ocular data for as many regions as possible.

It was further a central goal to evaluate the attained database regarding the usefulness of a glaucoma screening programme in Malawi or at LSFEH and define a guideline proposal for glaucoma management at LSFEH and possibly other tertiary institutions in Malawi. It is of interest, if the statement given in chapter 1.2.7 that population-based screenings are not useful (in Western countries) is equally true for developing countries. If IOP levels or prevalence of glaucoma in Malawi varied greatly from other settings, different conclusions regarding the usefulness of a screening programme in that region could be drawn. If for example the data set revealed that in Malawi, many people are found with highly elevated IOPs and large glaucomatous papillary excavations, this
could help in screening for and diagnosing the disease at an earlier stage than is possible e.g. European countries. Therefore, the dataset was analysed regarding these questions, also by relating the data back to the WHO criteria for a population-based screening mentioned in the previous chapter.

As suggested by Kyari et al. in review of literature on glaucoma in SSA: “More population-based research is needed to clarify the nature of glaucoma in many more populations in Africa, to determine reasons for its variation and to better define target risk groups.” (Kyari et al. 2013) The research therefore contributes to more knowledge and information about glaucoma in yet another region in Africa.
2 Materials and Methods

The following discourse first explains the instruments used for patient examinations throughout the studies. The second part outlines study designs, procedures and details about patient samples. Lastly, statistical analysis will be described.

2.1 Instruments for examination

This chapter gives an overview of instruments and material used for examining the study sample. Visual acuity assessment by visual chart and the tool for funduscopy is explained. Further, theory about optical coherence tomography and the two tonometers of this study are described.

2.1.1 Visual chart, indirect ophthalmoscopy and Anterior-segment Optical Coherence Tomography

Visual chart. To determine patients’ visual acuity, a tumbling E chart was used at 6 meter distance to the patient. As many patients were illiterate, this chart offers a useful tool. They were asked to tightly cover one eye with one hand and point to the direction or state to which direction the limbs of the E are pointing (up, down, left, right). This test was done under good lighting condition, for both eyes, if applicable. Visual acuity (VA) was examined relative to 6/6 (metres) with the following grades: 6/6, 6/9, 6/12, 6/18, 6/24, 6/36, 6/60, 5/60, 4/60, 3/60, 2/60, 1/60, hand movement (HM) and no perception of light (NPL).

Indirect ophthalmoscopy. Funduscopy was done by using a 90 dioptres funduscopy lens (Volk, USA) after dilatation of the pupil.

Anterior-segment Optical Coherence Tomography (ASOCT). The ASOCT used was a Slit Lamp Optical Coherence Tomography (SL-OCT™), Software Version 1.0.2.0 by Heidelberg Engineering. The instrument enables in vivo non-contact, high resolution imaging and measuring of anterior segment structures. Anterior chamber angles (ACA), anterior chamber depth (ACD), objective digital gonioscopy or thickness of cornea can be measured. Our study focused on CCT, ACD and ACA. Relevant information is
obtained, e.g. about angle configuration, saving patients from undergoing an unpleasant direct gonioscopy, which is further a subjective method in comparison to OCT.

The device consists of an OCT scanning unit combined with an HAAG-STREIT BD 900 Slit Lamp, a height-adjustable table, computer, monitor, keyboard, and mouse. It enables to store patient data and displays or prints images in grey scale or false colour.

The anterior segment OCT is technically based on the time-domain-OCT (TD-OCT)-interferometer with a mobile reference mirror. The OCT utilizes short-coherent infrared light from a superluminescence diode with a central wavelength of approximately 1310 nanometre. After leaving the source, the light beam is divided into two – one sample and one reference beam. While the sample beam enters the eye and is reflected, the reference beam traverses a delay line. Eventually, both beams are brought back together and the calculation of interferences results in the actual OCT-signal. The beam is directed across the eye, creates, and later combines several axial scans (A-scans), which give two-dimensional cross-sectional images, similar to ultrasound diagnostics. The reference mirror moves for each A-scan to determine the eye’s anatomical structure's depth. Scanning quality reaches a width of 15 millimetre (mm) and depth of 7 mm at a scanning speed of 200 Hertz. During measurement taking software quality checks ensure correct alignment for measurement accuracy. (Heidelberg Engineering 2008)

2.1.2 Goldmann-Applanation-Tonometer and ICare-Tonometer

Goldmann first described the method and limitations of tonometry which is still considered the gold standard. (Goldmann & Schmidt 1957) All types of tonometer applanate the cornea and correlate the force necessary to reach a certain level of deformity with intraocular pressure. As the tonometer presses against the ocular cornea, a corneal influence on the measurement technique and findings is evident. It is often complex to interpret the IOP findings, as they are dependent on many parameters, especially corneal configuration. (Neuburger et al. 2011) Furthermore, they are prone to different sources of errors, may it be examiner-, patient-, or instrument-based. (Rosentreter et al. 2011) Furthermore, it is true for all non-invasive IOP measurement techniques that the real IOP is not 100% known, unless it is correlated to an intracameral measurement of the same eye. (Boehm 2011) The following sections are an explanation of the two tonome-
ter used in this study, with a focus on examiner-, instrument-, or patient-associated sources of errors.

**Slit lamp and GAT.** The device used throughout the study was a Haag Streit Applanation-Tonometer AT 900 type R (BD-900). GAT is the gold standard in IOP assessment for more than 50 years. The ophthalmic physics which Goldmann based his technique on was the Imbert-Fick-law. It states that the power \( F \) necessary to applanate surface \( A \) of a sphere equals the product of existing intraspherical pressure \( P \) and the applanated surface \( A \) (\( F = P \times A \)). The law is valid for endlessly thin and perfectly spherical and flexible surfaces without any rigidity. These theoretical prerequisites, though, are only partly encountered in the human eye ball, which is not perfectly spherical, not endlessly thin, or flexible and has some volume changes during measurements. Further, the covering tear film possesses an inert tension, which pulls the tonometer probe towards the cornea. At least corneal rigidity \( B \) and capillary force of the tear film \( S \) have to be considered in the equation, resulting in a change of the Imbert-Fick-law: \( F = P \times A + (B - S) \). (Rosentreter et al. 2011) According to a written statement by an employee of Haag-Streit, the Imbert-Fick-law is incorporated in the device, yet hysteresis and corneal rigidity are not considered.

Goldmann first described his procedure in 1955. (Goldmann & Schmidt 1957) It uses a slit lamp with disinfected tonometer head and a double prism, using illumination through a cobalt blue filter. By adding fluorescent topical anaesthetics to the tear film, the corneal surface can be applanated by the examiner approaching the probe towards the cornea. Upon touching the surface with the tonometer front, a double prism optically divides the tear menisci into two green semi circles. Using a tension spring adjusted at the slit lamp, the applanated pressure can be finely adjusted until the two menisci touch one another on their inner margins. At this position, IOP can be read off the tension spring in mmHg. This method actually measures a force in meganewton (mN), not a pressure. Therefore, Goldmann calibrated the tonometer in grammeforce (1 grammeforce = 9.8 mN). When reading the tonometer results, 1 grammeforce is equated with 10 mN and directly indicated in mmHg. (Rosentreter et al. 2011)
It is important to add that there are various **sources of error** in this technique, which shall briefly be recorded here. Rosentreter et al. divide them into examiner-, instrument- or patient-associated influencing variables: (Rosentreter *et al.* 2011) Several factors can be responsible for **examiner-associated errors**. Firstly, applied anaesthetics for applanation can alter the pressure needed. Thus, a large amount of drops can result in higher measures and too little drops in lower values. The pressure applied by the examiner to help patients opening their eye, e.g. with cotton buds or touching eyelids or lashes with the probe, may result in falsely high values. Inaccuracy in reading off the results can occur due to the 2 mmHg range, which is seen on the tension spring. Further, the examiner may take slight eccentric measurements, repeat them several times or applanate the surface for more than 30 seconds, which can, according to the authors’ citation in their article, reduce the applanated IOP for 2 to 4 mmHg.

**Instrument-based errors** may result in systemic measurement errors. These can occur if calibration of GAT is not done regularly. Further, tonometer probes may be damaged, which leads to measurement inaccuracies and damage of the corneal surface.

Several patient-associated parameters have an influence on IOP and its readings, leading to **patient-based errors**. Pulse, breathing, or blink reflex can be visible as pulsating menisci. Bending forwards towards the slit lamp with reclusion of the neck, holding breath, or wearing tight collars may bring elevated venous pressure and IOPs. An increase in IOP levels of several mmHg can be explained by patients looking upwards during examination, especially those with endocrine orbitopathy, or forced activity of levator palpebrae muscle for intense opening of the eyes. Lastly, corneal characteristics, most importantly CCT, which is focused on within several levels in this thesis, play an important role in correctly interpreting IOP measurements. Corneal astigmatism can lead to imprecise GAT measures. Abnormal corneal epithelium is a current source of error. Oedematous epithelium is said to be applanated easier than normal epithelium and thus results in falsely low values. Thin CCTs and eyes after photorefractive surgery can lead to drastically lower IOP measurement. Opposing, thick CCTs rather result in high IOP values. (Rosentreter 2011) (Neuburger 2011) This phenomenon will be further elaborated in chapter 4.4 in the discussion of this thesis.
ICT. The tonometer used throughout the study was an Icare® TA01i by Icare Finland. The handheld instrument is based on the rebound phenomenon and was launched in 2003. Induction of rebound tonometry was developed in the end of the 1990s in Finland and quickly won recognition in the clinical routine. Its major advantage is that no special expertise and no local anaesthetics like in GAT are needed. The method is therefore readily accepted by children. The battery-driven, portable, handheld Icare® tonometer is one variant of rebound instruments present at LSFEH. During measurement a single-use tonometer head gets catapulted against the patient’s cornea, slowed down, and rebounds. Acceleration of the probe is induction-based through two coaxial inductors, whereas slowing down and mechanical rebounding is measured by changes in potentials. This is converted into intraocular pressure, appearing in digital readouts. The deceleration of the probe depends on the IOP. A higher IOP leads to a faster deceleration of the probe and a shorter contact time. Six measurements are taken, supported by acoustic signals, and a mean is generated and indicated as a digital number (P followed by IOP result), accompanied by a longer beep. (Boehm 2011) (Neuburger et al. 2011)

If there is an erroneous measurement, the tonometer will beep twice and display an error message. Thereby, different cases can occur: If “P” is blinking, standard deviation (SD) of the measurements is greater than normal. “P_” indicates SD of the different measurements has a slightly greater value than normal, but the effect on the result is likely to be irrelevant. “P-” means SD of the different measurements is clearly greater than normal, but may not have a relevant effect on the result, but a new measurement is recommended if the IOP is over 19 mmHg. “P” signals that SD of the different measurements is great and a new measurement is recommended. According to the producer, the effective range of the tool is 7 to 50 mmHg, but display range is from 0 to 99 mmHg, with the limitation that beyond the effective measurement range, IOP is only estimated. Its weight is 250 g including 4 batteries. (Icare Finland 2015)

The very light probe weighs 26.5mg, is 40 mm long, made of stainless steel, slightly magnetic, and provided with a 1.7 mm plastic covering at its top. Velocity of the probe towards the cornea is at 0.25-0.4 m/s, which is low enough not to harm the cornea, but faster than the corneal reflex. This explains why no anaesthetics are needed. Thereby,
the procedure is barely noticed by patients as only momentary contact happens. (Icare Finland 2012) (Hohmann 2011)

As indicated in the manufacturer’s manual, accuracy of the instrument with 95% tolerance interval relative to manometry is ±1.2 mmHg (≤20 mmHg) and ±2.2 mmHg (>20 mmHg). Repeatability (coefficient of variation) is <8%. According to literature, 84% of measurements are within ±3 mmHg variance compared to GAT, in a range of 6 to 48 mmHg. (Iliev et al. 2006) In comparison to GAT in general, ICare values tend to be 0.6 to 1.6 mmHg higher than GAT values. (Martinez-de-la-Casa et al. 2005) (Martinez-de-la-Casa et al. 2006) (Hohmann 2011) (Neuburger et al. 2011) (van der Jagt, Liane H. & Jansonius 2005) In the manual a mean paired difference and standard deviation (Goldmann-Icare) is given from a study with 158 patients with -0.4 mmHg and 3.4 mmHg. (Icare Finland 2015)

Obligatory for good measurement outcomes is a correct distance of the instrument to the cornea, central-orthogonal touching of the cornea by the probe, little tearing. Further, for correct interpretation, CCT should be known. ICT has to be applied in an upright position of the patient and held horizontally. A disadvantage is thus that it cannot be performed in patients lying in bed. For better positioning, a forehead support adjusting wheel is integrated. A major disadvantage is that in case of corneal pathologies like scars, rebound tonometry cannot be regarded as sufficiently accurate in its measurements. (Neuburger et al. 2011)

Since IOP control at certain individual target pressures is especially crucial for stopping the progress of the disease, a most accurate IOP determination is of utter importance. Despite many different measurement techniques and machines it cannot be said with certainty, if the measured IOP corresponds to the actual pressure inside the eye. (Boehm 2011) Only direct intracamereral measurements can indicate real pressures and comparative studies were done e.g. by Ehlers et al. and Kohlhaas et al. (EHLERS et al. 1975) (Kohlhaas et al. 2006) For ICT there are no intracamereral studies comparing ICT measurements to real IOPs, but it is reported by some authors that CCT, like GAT, may be influenced and dependent on CCT with up to 4 mmHg per 100 μm. (Boehm 2011) (Jorge et al. 2008) The ICare serves in the field of diagnosis, follow up, and screening
of glaucoma. (Icare Finland 2015) Its simple and fast applicability can explain the broad clinical acceptance.

2.2 Research design

For the literature research on existing studies and information on the topics of this thesis the PubMed US National Library of Medicine and publicly available online information were used.

The clinical research part consisted of three separate studies, each with own objectives and aims. Nevertheless, they had some identical features which will be described in the following lines. All three were cross-sectional studies and carried out between August and October 2014 at the outpatient department (OPD) of Lions Sight First Eye Hospital (LSFEH) in Blantyre, Malawi. LSFEH is the largest of five eye hospitals in Malawi, serving about 6 million people. It is under jurisdiction of Queen Elizabeth Central Hospital (QECH). LSFEH serves as teaching eye hospital for the College of Medicine as part of the University of Malawi. (Kayange et al. 2014)

As there is no computer-based patient documentation at LSFEH, we relied on patient’s narrative history and information given in their health passports, which every person in Malawi carries to each medical visit, containing a brief medical history and important diagnoses, such as tuberculosis or HIV status. All findings, e.g. IOP level or glaucoma diagnosis in these health passports, were documented and every book was marked with a coloured sticker to avoid double registration of this patient in the study.

Prior to the research we applied for ethical approval by the College of Medicine Research and Ethical Committee (COMREC) of Malawi in April 2014 and were granted admission in June 2014. (see appendix 9.4)

The following definitions and diagnostic guiding values were underlying:

IOP was considered “elevated/increased” at values above 21 mmHg in at least one eye. If available, pressure analysis was based on GAT-findings, the gold standard in tonometry. In other cases, IOP values were collected by ICT measurements.
In this setting with a limited availability of technical devices as visual field, good fundus photography and optic disc documentation such as OCT or HRT we had to rely on our clinical evaluation of the optic nerve head. Even though a CDR of $\geq 0.8$ is very suspicious for glaucoma we diagnosed those patients as “healthy” who had a large optic disc without focal thinning of the rim, optic disc haemorrhages and intact ISNT-rule. This was in accordance with the knowledge that the optic disc appearance varies between Caucasian and African, with African having larger discs with larger CDR. For example Nangia et al. describe that large optic discs are commonly found in black patients and might lead to an over-diagnosis of glaucoma. (Nangia et al. 2013) As the examinations were a subjective assessment we had to rely on the grading of our experienced African colleagues in cases of doubt regarding the diagnosis of glaucomatous optic neuropathy.

In our study people were diagnosed with glaucoma, if one of the typical features was present:

- Glaucomatous optic disc damage (abnormal inferior-superior-nasal-temporal (ISNT)-rule of the neuroretinal rim or abnormally large cup in a small optic disc) + IOP $\geq 22 \text{ mmHg}$ or
- IOP elevation above 35 mmHg without a corresponding nerve fibre defect or
- Optic nerve damage with a CDR $\geq 0.8$ that can be clinically related to glaucoma and is far advanced even without an elevated IOP (except those cases related to large optic discs (as mentioned above)

The diagnosis of “glaucoma suspect” was made according to the following criteria: (in accordance with (Pfeiffer 2005))

- IOP $\geq 22 \text{ mmHg}$
- VCDR $\geq 0.6$ with a normal disc size
- Diffuse or focal thinning of neuroretinal margin
- Papillary haemorrhages in accordance with glaucomatous optic neuropathy

The unavailability of visual field diagnostics made definitive diagnoses by perimetry impossible. Limitations are obvious since perimetry is a major diagnostic tool in
abovementioned definitions in 1.2.4. Therefore, a limited validity of the glaucoma diagnosis in the absence of perimetric data has to be taken into account. Like in other studies with limited technical options, CDR of the optic nerve head provided the base of staging severity of glaucoma. Asymmetry of CDR between both eyes was not considered suspicious as such, only in combination with suspicious optic disc appearance.

After giving clear definitions and explanations of the study design, the following chapters are descriptions of each of the three conducted studies. Study A was the first one, examining “healthy” Malawians. Study B was second in which ICT measurements were taken on a large scale. Study C consisted of thorough examination of those individuals referred from study B due to elevated IOPs.

2.2.1 Study A: Baseline survey

Objectives. The first study to be carried out was a two-week research period in August 2014 in which 200 people were examined. The aim of this study was to comprehensively examine patients with no history of high IOP or glaucomatous changes, or completely healthy individuals outside the hospital. The aim of examining “healthy” – meaning individuals without a history of glaucoma – was to gather data of average Malawian eyes as a baseline for further studies. Furthermore, results should indicate the prevalence of increased IOP above 21 mmHg and the number of glaucoma cases among them. Lastly, prevalence of glaucoma among patients with IOPs below 21 mmHg (NTG) was of interest.

Sample size. There is not much local data available regarding the prevalence of elevated IOP and glaucoma in this geographic area. With the collection of data from 200 “healthy” patients, no detailed description of the glaucoma prevalence and types was expected. It was rather considered a pilot study to collect baseline data and for interpreting consecutive studies. Since study A was a pilot study it was agreed on with the statistics office at the University of Tuebingen on the number of 200 patients. Not all parameters could always be collected of all 200 individuals, due to corneal ulcers, opaque discs or other ocular disturbances. The exact numbers of measurements can be cross-checked in appendix 9.3.2.
**Study population and inclusion criteria.** We recruited patients at the OPD and healthy individuals who were on the premises of the eye hospital, e.g. as “guardians” – usually family members of patients who accompany and care for the patient during the time of admittance. The main inclusion criteria were age above 18 without a history of glaucoma or increased IOP.

**Exclusion criteria.** Patients with the following features were excluded: known case of glaucoma, previous glaucoma surgery, patients on anti-glaucomatous medication, corneal abnormalities, e.g. ulcerations, scars etc. as they might interfere with measurements, children and young people below the age of 18 or lack of consent. Verbally given information was confirmed by cross-reading patients’ health passport in which medical data is recorded.

**Data collection.** Study subjects were asked to take part randomly. Before starting examinations, an information sheet and consent form were handed out (see appendix 9.5) explaining the necessary background of the study in simple words in English or the national language Chichewa. Afterwards patients had time to think about their participation and ask questions. Examinations were performed only after patients had agreed and signed the forms. For illiterate participants there was the possibility of giving consent by thumbprint.

Findings were collected on a questionnaire form (see appendix 9.5) in the following order:

- Ocular medical history: history of eye surgery, glaucoma and present complaint
- Monocular visual acuity (tumbling E chart) at 6 meter distance, if possible, in both eyes, and without correction; in case of low vision, the examiner tested finger-counting at 6 down to 1 meter distance (6/60 to 1/60), below 1 meter hand movement directly in front of the patient or light perception were tested
- ASOCT examination evaluating CCT, ACA, ACD
- Slit lamp examination of anterior chamber depth and condition of lens (clear, mild cataract, mature cataract, intraocular lens (IOL)), pigment dispersion. No exact grading of cataract other than mild or mature was done.
- IOP measured by ICT
• IOP measured by GAT
• Pupillary dilatation (after exclusion of the risk for occlusion or already closed ACAs with SL-OCT) by application of mydriatic eye drops, waiting 15 to 20 minutes for maximum dilatation
• Assessment of pseudoexfoliation (PEX) under slit lamp
• Assessing fundus and determining condition of the optic nerve head, particularly CDR and other pathologic findings

After finishing all examinations, patients were informed about results and given treatment if needed, including the prescription of medication, referral to further investigation and follow-ups, or admittance to ward. In those cases in which glaucoma was newly diagnosed, patients were thoroughly educated about the disease, implications, treatment, and importance of follow-up visits. Complete examination per patient took on average 30 minutes.

A local study assistant (final year medical student) recruited patients and explained the purpose and content of the study. He took history as well as visual acuity, and translated results and treatment to the patients. ACOCT and ICT were done by the author. Slit lamp examination by funduscopy and the final decision about diagnose and treatments were done by the German ophthalmologist Dr. med. Johanna Müller.

2.2.2 Study B: IOP assessment

Objectives. The second study aimed at getting a maximum number of IOP measurements at the OPD of LSFEH, to come up with a strong indicator for average IOP in a Malawian eye clinic, and the prevalence of increased ocular pressures.

Sample size. Because only little data is available regarding the prevalence of elevated IOP and glaucoma in this geographic area, it was a pilot study like study A to collect baseline data. ICT measurements of 1,112 patients in total were taken. As mentioned for study A, not IOPs could always be collected of all 1,112 individuals, due to ulcers or other corneal disturbances. The exact numbers of measurements can be cross-checked in appendix 9.3.3.
**Study population and inclusion criteria.** IOPs were measured by ICT on all patients above 18 years of age waiting in line at the OPD of LSFEH according to exclusion criteria.

**Exclusion criteria.** No ICT-measurements were taken in the following cases: corneal abnormalities, e.g. ulcerations, scars etc., children and young people below the age of 18, or lack of consent. There was no patient who denied the measurement. This broad IOP assessment also included patients with a known history of glaucoma. Information was taken from patient’s statements and health passports.

**Data collection.** Before collecting patient data, a local study assistant explained in simple words in Chichewa the purpose of our measurements, the concept of ocular pressure, and the risk of an unnoticed elevated pressure. Patients were encouraged to ask questions at any moment. They were informed that in case of pressures over 21 mmHg, a comprehensive eye examination (study C) would follow, in which their present complaints and also possible glaucomatous findings were looked at. Age, (family) history of eye disease or blindness, and ICT measurements were taken after each patient’s verbal consent. All examined patients received a sticker on their health passport to avoid double assessment in future OPD visits, and results were marked on a paper form as well as in the individual’s health book. In case of pressures above 21 mmHg ICT-measurements were repeated three times to rule out mistakes. If numbers were above 21 mmHg in at least one eye in all three measurements, patients’ health passports were marked with a red sticker. They were invited to proceed to a study room for comprehensive investigation, in which a thorough eye exam with special attention to elevated pressure and related pathologies would follow.

**2.2.3 Study C: Increased IOP examination**

**Objectives.** As described above, in a second step following ICT measurements of study B, examination was performed on all those with increased IOP in three consecutive ICT-measurements in at least one eye, who agreed to participate. This enabled to not only detect the prevalence of increased IOP at an OPD setting in Malawi (objective of study B), but also find out the actual prevalence of glaucoma or glaucoma suspects among those with increased pressures (objective of study C).
The focus on prevalence of glaucomatous findings among those with elevated pressures was aimed at getting results to further draw conclusions regarding the usefulness of an ICT screening at this or comparable settings.

By including patients with a history of glaucoma, a database was expected to be established with glaucomatous ocular findings to further investigate possible characteristics and correlations. For this purpose, the same details as in study A were registered on the questionnaire form (see appendix 9.5).

Sample size. The number of patients was determined continuously by findings of study B. In total 106 patients, who presented with ICT measures above 21 mmHg in study B, were included and fully examined. As valid for studies A and B, not all parameters could always be collected of all 106 individuals, due to corneal ulcers, opaque discs or other ocular disturbances. The exact numbers of measurements can be cross-checked in appendix 9.3.4.

Study population. All 154 patients of study B who presented with IOP above 21 mmHg in three consecutive ICT measurements in at least one eye were encouraged to join. 106 of those joined the study.

In- and exclusion criteria. Criteria for in- and exclusion were the same as in study B as this was the continuation. Due to lack of time or scepticism on the patient’s part, not every patient meeting inclusion criteria was examined.

Data collection. In the course of study B, patients were already informed by a Malawian study assistant (Herbert Thole or Boston Zimba) about the research and the meaning of an IOP above 21 mmHg. Patients with this certain finding were asked to join for a comprehensive examination in a separate study room. They were then given further explanations and had to sign (with thumbprint if illiterate) the same consent form as in study A (see appendix 9.6).

Examinations and data collection followed the order of study A and were noted on the same form (see appendix 9.5). After explanations, history taking, and visual acuity, followed ASOCT picturing, slit lamp examination including GAT and administration of
mydriatic eye drops. Funduscopy for CDR evaluation and final diagnosis with treatment were made by Malawian ophthalmologists.

2.3 Statistical Analysis

All data was treated confidentially and is kept in a password-protected file. All study data was recorded on standard questionnaire forms, checked for completeness, and entered into a database sheet using Microsoft Office Excel 2010.

Data included the date of examination, patient number (assigned by author), gender, and age. Examination findings included VA, subjective ACD and lens in slit lamp examination, IOP measurements with ICT and GAT, presence of PEX or pigment dispersion, lens, fundus, CDR of the optic disc, as well as ACA, ACD and CCT by SL-OCT examination.

All data was exported to IBM SPSS Statistics Version 22. Subgroups were formed in SPSS, including female or male gender, patients above and patients below 40 years, patients with CDR above 0.8 or glaucoma diagnosis among others.

Results were evaluated in mean, median, standard deviation, minimum-maximum-ranges, frequencies, or percentages. All relevant variables were examined for normal distribution. If a normal distribution was not given, as in many cases, median and range with minimum and maximum are indicated. All relevant results were transferred to Excel sheets.

Descriptive analysis of all relevant variables was done, followed by Spearman bivariate correlational analysis between age, IOP, CCT, and CDR using SPSS programme. Spearman (rho) was considered appropriate due to the non-normal distribution of at least one variable in all correlations. A correlation of -1.0 to -0.5 or 1.0 to 0.5 was considered strong, -0.5 to -0.3 or 0.3 to 0.5 moderate and between -0.3 and -0.1 or 0.1 to 0.3 was considered as weak, whereas values between -0.1 and 0.1 meant no correlation.

Further, sensitivity and specificity as well as positive and negative predictive value were calculated for study A regarding ICT detection of glaucoma cases.
Bland-Altman-analyses were carried out for the comparison of measurements generated by the two tonometry methods (ICT and GAT) and depicted in scatter-plots (see chapter 3.6).

Statistical analyses and results are presented in the form of tables or bar graphs as applicable.

In accordance with the German statistical consultant, no statistical tests with non-metric variables were done. The reason is that sample size estimations were not possible in advance due to the lack of available data for this region. Consecutively, testing would result in high error rates, depriving the study of its persuasive power. We therefore only calculated correlations and summarized the descriptive statistics, which can give rise to further studies and research in the future.
3 Results

The following chapters present the results of each study separately with their specific focus and questions. Ocular characteristics and study findings are presented and analysed. In study A and C these are age and gender distribution, IOP levels with prevalence of increased IOPs, CCT, CDR, ACD, ACA, VA and blindness, cataract and prevalence of glaucoma. In study B, main findings are gender and age distribution, IOP levels and the prevalence of increased IOP levels.

POAG is the most prevalent glaucoma type in SSA. Therefore this subtype was focused on during the research of this study. All POAG patients with their specific patterns are combined in chapter 3.4. This allows a detailed analysis of POAG presentation patterns in Malawi. A special focus is put on glaucoma presentation patterns. Possible correlations between metric parameters, such as age, IOP, CCT, or CDR are analysed in chapter 3.5. Furthermore, Bland-Altman-analysis is done to compare ICT with GAT measurements, with possible implications on ICT cut-off points, as outlined in chapter 3.6.

The division of visual impairment and blindness follows the ICD-10 definitions described in chapter 1.1.2. Certain age group structuring was applied, which is briefly explained as follows: Group 1 comprised people of 18 to 24 years of age. 18 years was the minimum age for inclusion in all studies. The upper limit of 24 years was chosen, because 25 is mentioned in literature, e.g. in (Essuman & Ntim-Amponsah 2012), as a good age to start screening. It is part of the discussion in chapter 4.5.2. For comparative reasons, this cut between 24 and 25 was set.

Group 2 was formed by people between 25 and 39 years of age, because comparable studies, which are also part of chapter 4.5.2, e.g. (Ntim-Amponsah et al. 2004) or (Ntim-Amponsah et al. 2005), often contrast samples below and above 40 years. For comparative reasons, 39 years was regarded an appropriate cut-off point.

Group 3 included ages 40 to 59, as this was equally seen in comparable studies, e.g. (Kyari et al. 2013). Group 4 was formed from ages 60 to 79, and group 5 from 80 years and above. The last two categories have been chosen for comparable age ranges. These two were the smallest samples due to low life expectancy in Malawi, which is 58 years.
for men and 60 years for women. (WHO 2012b) Results of study A, B, C, and of POAG patients are summarized in Table A 1 of the appendix under 9.3.1, which can be used for orientation and comparison.

3.1 Study A: Baseline survey, “healthy” sample

As explained in chapter 2.2.1, the aim of study A was to gather data of Malawian eyes as baseline for further studies. Therefore, allegedly healthy individuals, with “healthy” meaning no history or unaware of high IOP or glaucomatous changes, were comprehensively examined. Furthermore, prevalence of IOPs above 21 mmHg, and the number and types of glaucoma cases detectable during a random screening of a “healthy” sample were determined. The full list of results from study A is attached in appendix 9.3.2.

3.1.1 Description of sample size, gender ratio, age distribution, mean IOP, CCT, CDR, ACA, cataract and visual acuity

A total number of 200 “healthy” individuals without a known-history of glaucoma were randomly recruited on the hospital premises (if meeting inclusion criteria) for a thorough eye examination. As mentioned in 2.2, due to ulcers, scars or other corneal opacities, the number of measured right eyes was 191 and of left eyes it was 188. (Compare appendix 9.3.2)

Table 4 summarizes the main findings. These parameters can serve as a baseline of ocular parameters for the Malawian population.

The sample consisted of 53% women (number (n) =106) and 47% men (n=94). The rather equal distribution was aimed for by the researchers in order to avoid bias for one gender and to get equal amounts of baseline data on each.

The mean age was 35.3 years (median 32; range 18-78), where a majority of 67.5% belonged to the group of under 40 years and 32.5% were 40 years or older.

Figure 1 shows the distribution of age groups in study A. Almost half of all people (47.5%) represented group 2 (25-39 years), whereas 20% formed group 1 (18-24 years), 26% group 3 (40-59 years), 6.5% group 4 (60-79) and none in group 5 (80 years and above).
Table 4: Main ocular findings in healthy Malawian population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td></td>
<td>200</td>
</tr>
<tr>
<td>Gender distribution (male : female)</td>
<td>%</td>
<td>47 : 53</td>
</tr>
<tr>
<td>Age mean / median</td>
<td>Years</td>
<td>35.3 / 32</td>
</tr>
<tr>
<td>IOP (ICT/GAT) mean</td>
<td>mmHg</td>
<td>16.6 / 15.4</td>
</tr>
<tr>
<td>IOP (ICT/GAT) median</td>
<td>mmHg</td>
<td>16 / 15</td>
</tr>
<tr>
<td>IOP &gt;21 mmHg</td>
<td>%</td>
<td>11.5</td>
</tr>
<tr>
<td>CCT mean / median</td>
<td>µm</td>
<td>509.2 / 507.5</td>
</tr>
<tr>
<td>CDR mean / median</td>
<td></td>
<td>0.3 / 0.3</td>
</tr>
<tr>
<td>CDR &gt; 0.8 (at least one eye)</td>
<td>%</td>
<td>2.0</td>
</tr>
<tr>
<td>Cataract bilateral</td>
<td>%</td>
<td>16.3</td>
</tr>
<tr>
<td>Blindness unilateral / bilateral</td>
<td>%</td>
<td>1.0 / 0</td>
</tr>
<tr>
<td>Glaucoma prevalence</td>
<td>%</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Figure 1: Age group distribution in percentages of healthy sample, n=200; age group 1 (18-24 years), 2 (25-39 years), 3 (40-59 years), 4 (60-79)
IOP was measured first with ICT and then with GAT, which is indicated as ICT/GAT. Mean ICT and GAT values for right eyes were 16.5/15.3 mmHg (median 16/15, range 8/8-31/27 mmHg) and in left eyes 16.6/15.5 mmHg (median 16/15, range 10/9-51/53 mmHg) respectively. In conclusion, total mean for both eyes in ICT/GAT was 16.6/15.4 and median in ICT/GAT was 16/15 mmHg. ICT values of over 21 mmHg in at least one eye were recorded in 11.5% and above 22 mmHg in 10%.

CCT measurements in both eyes showed normal distribution. Mean CCT in 190 right eyes was 509 µm (SD 35.7) and in 188 left eyes 509.5 µm (SD 37.1). Total mean CCT for both eyes was 509.2 µm. Total median was 507.5 µm.

Figure 2 and Figure 3 shows CCT distributions for both eyes separately. As the difference between eyes did not show a clinical significance in the examined parameters, both eyes are regarded together in the on-going text.

![Central Corneal Thickness Distribution](image.png)  
*Figure 2: Right eye, central corneal thickness (CCT) in healthy study population, n=108, frequency numbers (no.)*
CDR assessment gave a left-skewed distribution. Mean as well as median CDR in both eyes was 0.3 (right eye range 0.1-0.8, left eye range 0.1-1.0). The amount of patients with at least one eye presenting with a CDR of 0.8 or worse was 2% (n=4).

In those four people with a minimum CDR of 0.8, 50% (n=2) were newly diagnosed with glaucoma, and 25% (n=1) were declared suspects. Furthermore, the mean age of those with CDR of at least 0.8 was 56 years (median 61, range 23-78), the presence of bilateral cataract was high (75%). Mean and median ICT/GAT-values were higher than in the average sample (mean ICT/GAT of 20.1/19.5 mmHg versus 16.6/15.4 and median ICT/GAT of 17.8/17.3 mmHg versus 16/15 mmHg).

ACD mean in both eyes was 2.95 mm (SD 0.3 both eyes). ACA means for all angles (nasal, temporal) in both eyes were 38° (range 18-60°). 16.3% (n=31) of people presented with bilateral cataract. As described in chapter 2.2.1, no exact grading of cataract other than mild or mature was done.

Regarding visual acuity, no patient was bilaterally blind. All 190 right eyes (100%) studied had a vision of 3/60 or better. 99% of 188 left eyes had 3/60 vision or better.
only 1% (n=2) presented with left eye, unilateral blindness with visual acuity of less than 3/60, one with hand movement and one with NPL.

3.1.2 Glaucoma prevalence and types in healthy study sample

In an initially “healthy” sample of 200 people, five (2.5%) of these were newly diagnosed with glaucoma. POAG was the leading subtype with 60%, PEX and NTG formed 20% each. Out of the 23 patients detected by the ICT with IOPs above 21 mmHg four patients were finally diagnosed with glaucoma, whilst the NTG was by definition not detected by the ICT. Table 5 shows the subdivision.

<table>
<thead>
<tr>
<th>Glaucoma</th>
<th>Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive test result</td>
<td>4</td>
</tr>
<tr>
<td>Negative test result</td>
<td>1</td>
</tr>
</tbody>
</table>

This corresponds to ICT sensitivity in detecting glaucoma by increased IOP levels (above 21 mmHg) of 80% with a specificity of 90%. Yet, the positive predictive value (PPV) of the ICT was only 17% and the negative predictive value (NPV) 99.4%. This result is due to the very few positives compared to many negatives, which needs to be taken into consideration when interpreting these results.

Another five (2.5%) of all were marked as glaucoma suspicious due to their ocular findings and advised for follow up visits. This adds up to 5% (n=10) glaucomatous people among the “healthy” sample.

All definitive POAG cases of study A and C combined are analysed separately in chapter 3.4 to represent a larger sample, and exclude secondary glaucoma cases with very different findings, leading to distortion of the data regarding e.g. cornea, vision, and IOP.
3.1.3 Study A excluding glaucomatous eyes

Study A was an allegedly healthy – meaning non-glaucomatous – sample, among which 2.5% (n=5) glaucoma cases and 2.5% (n=5) glaucoma suspects were newly diagnosed.

Discounting these ten individuals from the sample, results in a data set which is 100% non-glaucomatous. Thus it was thought to represent the Malawian non-glaucomatous population better than the original sample A, which included some glaucomatous eyes. The same data analysis was done on the remaining 95% of the original data set to see possible differences. However, results were similar. As there was only a minor difference between 100% “healthy” and 95% healthy sample, all further descriptions of study A refer to the full data set including five glaucoma cases and five suspects, if not said otherwise.

Gender distribution was almost equal with 54.7% females and 45.3% males. Median age was the same (32 years), as well as age group distribution. IOP medians were also equal to the original data, but instead of 11.5%, only 9.5% had increased IOP levels.

The median CCT value with 506.8 µm was slightly thinner than in the full sample (507.5µm). Bilateral cataract was less prevalent in the non-glaucomatous data set (14.7% instead of 16.3%).

3.1.4 Characteristics and glaucoma prevalence in patients with raised IOP

11.5% (n=23) in the non-glaucomatous, healthy study sample presented with an IOP of over 21 mmHg. 52% were female and 48% male. Mean age was 41 years (median 39; range 22-78), compared to 35.3 years in the total sample. Equally to the total sample, almost half of all (47.8%) belonged to age group 2 between 25 and 39 years.

Median ICT/GAT-values were 23/20.5 mmHg. Median CCT for both eyes was 515µm (right range 440-613; left range 434-610), which was thicker than that of the total sample (507.5 µm) described in chapter 3.1.1. A median CDR of 0.3 was found in both eyes, which equals the complete sample. Twenty-four percent showed cataract in both eyes and 9% of people presented with unilateral blindness, which was clearly higher than the 1% in the total healthy sample.
Whereas 2.5% of the whole study sample was diagnosed with glaucoma, in the group of elevated IOPs the proportion was 17.4%. This finding gives incentives for further discussion regarding the usefulness of ICT screening, as discussed in chapter 4.5.1 and chapter 4.6.

### 3.1.5 Comparison between gender and different age groups

The intended equal proportion of **male to female** participants (47:53) allows the comparison of results. Female median age was 35 years (mean 35.1; range 18-64), male median age was 31 years (mean 35.5; range 18-78). Females over 40 years were 34.9%, while males over 40 years represented 29.8%. Age group distribution by gender is illustrated in Figure 4. In summary, men exceeded women in the young age group between 25 and 39 years and also in the age group above 60 years.

![Figure 4: Age group distribution by gender in study A (%)](image)

Median IOP of males was in average 1 mmHg above female values. Median IOP in male eyes was 16.5/15.3 mmHg in ICT/GAT (range 8-53) versus 16/14 mmHg in ICT/GAT of female eyes (range 8-29). Both genders showed the same proportion of people above 21 mmHg in at least one eye, with 11.7% of men and 11.3% of women.
Mean CCT values did not vary much between genders, although males had slightly thinner CCT median values. In median values males had 505 µm and females 508.4 µm. ACD and ACA means were similar between genders. ACD in both eyes of males was 3.0 mm, for women it was 2.8 mm for both eyes. ACA means for males were 38 to 39°, and in females 36 to 38°. CDR medians in both genders were 0.3, while 1% of women and 3.4% of men showed CDR of 0.8 or more in at least one eye. No major difference was detectable in the presence of cataract or visual impairment.

Despite finding only five glaucoma cases, the gender distribution was strongly unequal. Four out of the five cases were male, representing 4.3% of all men and 0.9% of all were women. Also among suspects the gender ratio varied, with 4.3% and 0.9% respectively.

Comparing features of participants above and below the age of 40 demonstrated more differences than comparing gender. There were slightly more females (56.9%) in the group over 40 years compared to men (43.1%), than in the group below 40 (51.1% female versus 48.9% male). IOPs did not differ much in both groups with medians around 15 and 16 in both groups. Nevertheless, more over 40 than below age 40 presented with IOPs above 21 mmHg (13.8% versus 10.4%). CDR median in both groups was 0.3.

Large differences appeared in the remaining features, in which the elderly showed lower and respectively worse values. Median CCT values of those below 40 years was 509.5 µm (range 428-613), whereas in those over 40 years CCT was lower with median 502 µm in both eyes (range 423-582). Mean ACDs in the older group was lower, with 2.8 mm versus 3.0 mm in the younger. ACAs were narrower, with means of around 34-35° in the older group and 38-40° in the younger group. As cataract is a phenomenon mainly of age, a difference was also seen in these two groups. Twenty-four percent had cataract in both eyes in the group over 40 years, against 5% in the younger group. Vision in both groups was mostly above 3/60. Only in the group above 40 years of age, there was 3% with unilateral blindness with vision below 3/60.

A large gap could be seen in terms of new glaucoma diagnosis. Whereas 1.5% of those younger than 40 years were newly diagnosed, in those above 40 it was 4.6%. In summary, elderly individuals presented with more advanced findings concerning VA, cata-
ract, and CDR, and were more often diagnosed with glaucoma. The following chapter 3.1.6 is a concluding summary, joining the most important findings of study A.

3.1.6 Summary of study A

Study A resulted in baseline data of 200 healthy, non-glaucomatous Malawian patients, with 400 eyes. The study population had an almost 50:50 male-female ratio. Mean age was 35.3 years (median 32; range 18-78), with 67.5% belonging to the group of under 40 years. Total mean for both eyes in ICT/GAT was 16.6/15.4 mmHg and median in ICT/GAT was 16/15 mmHg. The prevalence of increased IOP in the healthy sample was 11.5%.

Mean CCT for both eyes was 509.2 µm, median was 507.5 µm. Mean as well as median CDR in both eyes was 0.3. The number of patients with at least one eye presenting with a CDR of 0.8 or worse was 2%, with a mean age of 56 years. Of those with CDR of 0.8 or worse, 50% were newly diagnosed with glaucoma, 25% were suspects and 25% were classified as healthy. No patient was bilaterally blind.

2.5% of study A was newly diagnosed with glaucoma, where POAG was the leading subtype with 60%. Another 2.5% of all were glaucoma suspects. Of the 11.5% presenting with ICT-levels above 21 mmHg, 17.5% were diagnosed with glaucoma. This corresponds to ICT sensitivity in detecting glaucoma by increased IOP levels (above 21 mmHg) of 80% with a specificity of 90%. The PPV of the ICT was 17% and the NPV 99.4%.

Looking at those with glaucoma diagnosis, median CCT was slightly thicker (515 µm than in the total sample of study A (507.5 µm). Median age (39 versus 32 years) was higher in those with glaucoma diagnosis versus the total sample.

Men and women did not differ much in terms of ocular parameters such as IOP, CCT, or CDR. A difference though existed in the proportion of males and females diagnosed with glaucoma, which was a 4:1 male-female ratio. This indicated a male majority in this subgroup, although the number of cases was too small to deduce a general statement from it.
Differences were detected when comparing individuals below and above 40 years of age. Those above 40 presented with thinner CCT, narrower ACAs, less ACD and lower VA, as well as more cataracts. In terms of new glaucoma diagnosis, 1.5% of younger 40 years were newly diagnosed, while in those above 40 it was 4.6%.

3.2 Study B: IOP assessment

After the thorough eye examination of study A, the aim of study B was to get a maximum number of IOP measurements at the outpatient department (OPD) of LSFEH. This was meant to generate a strong indicator for the average IOP, and the prevalence of increased ocular pressures in Malawian patients at an eye clinic. A summarized list of findings is attached in 9.3.3 of the appendix.

3.2.1 Description of sample size, gender ratio, age distribution and mean IOP

The IOP of 1,112 patients at the OPD of LSFEH were measured with an ICT. As mentioned before, due to ulcers and other corneal disturbances, 1,099 right eyes and 1,090 left eyes were measured (compare appendix 9.3.3). Age, gender, and IOPs were documented for both eyes. Main findings are summarized in Table 6.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>No.</td>
<td>1,112</td>
</tr>
<tr>
<td>Gender distribution (male : female)</td>
<td>%</td>
<td>41.8 : 58.2</td>
</tr>
<tr>
<td>Age mean / median</td>
<td>Years</td>
<td>41.2 / 36</td>
</tr>
<tr>
<td>IOP (ICT) mean</td>
<td>mmHg</td>
<td>16.6</td>
</tr>
<tr>
<td>IOP (ICT) median</td>
<td>mmHg</td>
<td>15.5</td>
</tr>
<tr>
<td>IOP &gt;21 mmHg</td>
<td>%</td>
<td>13.8</td>
</tr>
<tr>
<td>New glaucoma diagnosis</td>
<td>%</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Gender distribution at the OPD was 58.2% females and 41.8% males. The average age was 41.2 years (median of 36 years) with a minimum of 18 and an alleged maximum age of 112, as claimed by the patient and her attenders (without proof of birth certificate). The distribution within the defined age groups is seen in Figure 5: Age group 1
from 18 to 24 years of age were 17.4%, group 2 from 25 to 39 years was 38.1%, group 3 from 40-59 years represents 25.4%, group 4 from 60-79 years was 17.1% and group 5 from 80 years onwards comprised 2% of patients.

Mean age of women was 40 years and of men 42.8 years, whereas 42% of women and 48% of men were older than 40 years. As in study A, the difference between both eyes showed no clinical significance so that they will be described together in the text below. Total mean/median ICT for both eyes was 16.6/15.5 mmHg (range 3-81). The prevalence of patients with raised ICT values above 21 mmHg was 13.8% and will be further described in chapter 3.2.3.

3.2.2 Glaucoma presentation patterns, known and new diagnosis

3.1% of patients (n=34) seen at the OPD had a known history of glaucoma. Of those 34 patients, male-female ratio was 59:41, opposing the 40:60 distributions in the total study population. Thus results showed a male dominance.

Known glaucoma patients on average were older. Mean age was 58.2 years (median 62; range 18-81), with 11.8% below the age of 40 and 88.2% above. Their mean IOP was 30.8 mmHg and median was 26 mmHg.
Anticipating the results from the thorough examination of study C, a total of 2.4% (n=27) of all 1,112 patients were newly diagnosed in the study with glaucoma. The mean age of those 27 new glaucoma patients was 53 years. Another four out of the 1,112 patients were seen by other specialist and also newly diagnosed with glaucoma, making 2.7% of the OPD population.

### 3.2.3 Characteristics and glaucoma prevalence in patients with raised IOP

The vast majority of all 1,112 OPD patients presented with ICT values below 21 mmHg. The prevalence of patients with raised ICT values above 21 mmHg was 13.8%, as mentioned in chapter 3.2.1, whereas not all could be fully examined afterwards. 9.5% (n=106) instead of 13.8% (n=154) received full eye examinations.

Of those 154 patients with raised IOPs, 46.8% were female and 53.2% were male. So despite the fact that there was a female majority in the OPD pool, male gender had a tendency to present more often with IOP values above 21 mmHg.

The mean age of all 154 patients with increased IOP was 47.9 years (median 47; range 18-82 years; SD 18.04). A majority (61.7%) was in the age group of 40 years and above. Another age division showed that age groups 2-4 (group 2 (25-39 years): 26.6%; group 3 (40-59 years): 27.9%; group 4 (60-79 years): 32.5%) approximately comprised one third of all patients each. Only 11.7% fell into group 1 (below 25 years) and 1.3% into group 5 (from 80 years onwards), which was also the smallest study population due to the low life expectancy in the country. This distribution among the five age groups is illustrated in Figure 6 and can give possible hints as in how to structure screening programmes.
In those 154 individuals with elevated ICT measurements mean IOP was 27.7 mmHg (median 25; range 6-81). About one fifth (20.9%, n=32) of those found with raised IOPs at the OPD already had glaucoma diagnosed and mostly had IOD values far above 21 mmHg, while only two known glaucoma patients had an IOD below 21 mmHg. Of those 106 patients who were fully examined and included in study C, 25.5% (n=27) were later newly diagnosed with glaucoma. These results will be discussed in chapter 4.5.

3.2.4 **Comparison between gender and different age groups**

The comparison of males and females showed a slightly higher age of males presenting at the OPD. The mean age of men was 42.8 years (median 38; range 18-87) and 40.0 years in females (median 35; range 18-112). 40.6% of women were found in age group 2 (25-39 years) and 34.6% of men, while male patients were better represented in the older age groups. The age group 4 (60-79 years) had 20.2% male and 14.8% female patients. In age group 5 (80 years onwards) males were twice as many as females (2.8% versus 1.4%).
Whilst 4.3% of men indicated a known glaucoma diagnosis, only 2.2% of women did so. Whereas 17.6% (n=82) of all males presented with increased IOP above 21 mmHg, elevations were only found in 11.1% (n=72) of women. Accordingly, more males (11.2%) than females (8.3%) were fully examined and included in consecutive study C. Nevertheless, no difference was found in the median ICT values, with 15.5 mmHg in both genders.

**In respect to age above and below 40**, in the group below 40 years 60.8% were women and 39.2% were men. The group above 40 years consisted of 54.9% females against 45.1% of males. ICT median was 15.5 mmHg in both age groups. The mean ICT value in the group above 40 years was higher with 17.3 mmHg (range 3-81) in those above 40 years against 16.0 mmHg (range 3-61) in the younger age group.

In terms of elevated IOP readings, the age group of 40 and above showed a stronger tendency for elevated values. In this group 19.2% came with IOP elevations, while in those below 40 years 9.6% had elevated IOPs. Correspondingly, the number of people with known glaucoma was higher in the elderly patients, with 6.1% of people above 40 years against 0.6% of patients under 40.

### 3.2.5 Summary of study B

In study B – the IOP assessment among 1,112 patients at the OPD - gender distribution was 58.2% female and 41.8% male. The average age of study B was 41.2 years. Women presented at a younger age with 40.6% between 25 and 39 years against 34.6% of men. Adding up the two age groups of 18 to 24 years with 25 to 39 years results in 57.9% women and 52% men, which shows an overall younger female study sample.

Total mean/median for both eyes was 16.6/15.5 mmHg respectively. The prevalence of patients with raised ICT values above 21 mmHg was 13.8%, while male gender had a higher tendency to present with IOP values above 21 mmHg. The mean age of all with increased IOP was 47.9 years, and age groups 2 to 4 each comprised approximately one third of all patients (25-39: 26.6%; 40-59: 27.9%; 60-79: 32.5%).
About one fifth (20.9%, n=32) of those found with raised IOPs at the OPD already had glaucoma diagnosed and most had IOD values far above 21 mmHg, while only two known glaucoma patients had an IOD below 21 mmHg.

3.1% of patients had a known history of glaucoma, with male dominance (male-female ratio of 59:41). Known glaucoma patients on average were older, with a mean age of 58.2 years, as 88.2% were above the age of 40. Their mean IOP was 30.8 mmHg and median was 26 mmHg for both eyes. A total of 2.4% (n=27) of all 1,112 patients were further on diagnosed in study C with glaucoma at a mean age of 53 years.

In respect to gender, males at the OPD presented at a higher age (median 38 versus 35 years in female), whereas the median ICT was equal (16 and 15 mmHg) in both genders. In total numbers, more males than females presented with known glaucoma (4.3 versus 2.2%), or elevated IOPs above 21 mmHg (17.6 versus 11.1%). In retrospect, also more male patients were newly diagnosed with glaucoma (3.4 versus 1.7%).

Regarding the difference in patients below or above 40 years of age, it can be seen that older patients showed a higher IOP mean of 17.3 mmHg against those below 40 years with 16.5 mmHg. Medians for both groups were 15.5 mmHg. More people above 40 years (19.2%) than below (9.6%) presented with elevated IOPs.

The association between glaucoma and age was underlined by the average age of people with a known glaucoma diagnosis of 58.1 years. Further, 1.1% of those below 40 years against 4% of those over 40 years were later diagnosed with glaucoma.
3.3 Study C: Increased IOP examination

In a second step following ICT measurements of study B, all those with increased IOP above 21 mmHg were comprehensively examined to find out the actual prevalence of glaucoma, or suspects among those with increased pressures. A detailed documentation of results is added in 9.3.4 of the appendix. For a short comparison see Table 7.

One aim of this study was to draw conclusions regarding the usefulness of an ICT screening at this specific setting, which is part of chapter 4.5. By including patients with a history of glaucoma, a database to investigate possible characteristics and correlations in glaucomatous eyes was established.

3.3.1 Description of sample size, gender ratio, age distribution, mean IOP, CCT, CDR, ACA, cataract and VA

A total of 154 patients were referred to take part in study C. These were detected with IOPs of over 21 mmHg during the large IOP assessment of study B. As described in chapter 3.2.3 due to logistical reasons (lack of time or unwillingness of patients), 106 instead of 154 individuals with increased IOP received full eye examinations. As also previously mentioned, not all parameters could always be collected of all 106 individuals, due to corneal ulcers, opaque discs or other ocular disturbances. The exact numbers of measurements can be cross-checked in appendix 9.3.4.

The sample of study C consisted of 50.9% women (n=54) and 49.1% men (n=52). This almost 50:50-distribution occurred randomly without intention. The sample also included 12.3% (n=13) with a known history of glaucoma, as this helped in collecting more data on glaucomatous eyes in this setting, as mentioned in 2.2.3. The main findings of study C are summarized below in Table 7. Mean age was 46.6 years (median 43 years; range 19-81), of which 41.5% belonged to the group under 40 years and 58.5% to the group of 40 years or older. According to age groups, 13.2% formed group 1 (18-24 years), whereas about one third made up group 2 (25-39 years: 28.3%), group 3 (40-59 years: 28.3%) and group 4 (60-79 years: 29.2%). A minor part (0.9%) was found in group 5 (80 years and above). The distribution was thus comparable to the one found in study B (shown in chapter 3.2.3), which sample C is formed of.
Table 7: Main ocular findings in study C, people with IOP > 21 mmHg

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>No.</td>
<td>106</td>
</tr>
<tr>
<td>Gender distribution (male : female)</td>
<td>%</td>
<td>49.1 : 50.9</td>
</tr>
<tr>
<td>Age mean / median</td>
<td>Years</td>
<td>46.6 / 43</td>
</tr>
<tr>
<td>IOP (ICT/GAT) mean</td>
<td>mmHg</td>
<td>26.7 / 25.9</td>
</tr>
<tr>
<td>IOP (ICT/GAT) median</td>
<td>mmHg</td>
<td>24.5 / 24</td>
</tr>
<tr>
<td>CCT mean / median</td>
<td>µm</td>
<td>527.8 / 527</td>
</tr>
<tr>
<td>CDR mean / median</td>
<td></td>
<td>0.45 / 0.4</td>
</tr>
<tr>
<td>CDR &gt; 0.8 (at least one eye)</td>
<td>%</td>
<td>18.7</td>
</tr>
<tr>
<td>Cataract bilateral</td>
<td>%</td>
<td>28.3</td>
</tr>
<tr>
<td>Blindness unilateral</td>
<td>%</td>
<td>21.7</td>
</tr>
<tr>
<td>Blindness bilateral</td>
<td>%</td>
<td>3.8</td>
</tr>
<tr>
<td>Glaucoma prevalence</td>
<td>%</td>
<td>25.5</td>
</tr>
</tbody>
</table>

Among all 106 patients mean ICT/GAT-values for both eyes were 26.7/25.9 mmHg (range 11-81) and the median was 24.5/24 mmHg. Total median CCT for both eyes was 527 µm respectively. This was higher than the median CCT-values in the healthy study sample of study A (507.5 µm).

Excavations of the optic disc were slightly larger than in healthy eyes, with median CDR of 0.4 (compared to 0.3). 18.7% showed CDRs of 0.8 or worse against 2% in sample A. Of those with a CDR of 0.8 or more, 50% were diagnosed with glaucoma according to the definition given in 2.2. Their optic nerve damage could be clinically related to glaucoma or was far advanced even without an elevated IOP. As discussed in 2.2 the optic disc appearance in Africans differs from the one in Caucasians in the sense that they are often larger and thus have a bigger excavation. (Nangia et al. 2013) In accordance to the opinion of our African colleagues, who are more familiar with the optic disc appearance of the Malawian population, they were classified as non-glaucomatous optic discs but were advised to come for follow ups.

ACD and ACA did not show different results to the healthy sample. Mean ACD was 2.8 mm for both eyes and ACA means clustered around 38° (range 0-68°). Unilateral blind-
ness (VA less than 3/60) was present in 21.7% (39% in the right eye, 61% in the left eye). 3.8% (n=4) were bilaterally blind.

As mean age was higher, there was a large portion of people with cataract. 28.3% had bilateral cataract, of which 40% were diagnosed with glaucoma, 23.3% already had glaucoma diagnosed, and another 10% were glaucoma suspects or known suspects. This large percentage of people with common cataract and glaucoma gives implication for discussion in chapter 4.5.3.

3.3.2 Glaucoma prevalence and types in raised IOP sample

In this sample of 106 people, 25.5% (n=27) were newly diagnosed with glaucoma and 12.3% (n=13) already had glaucoma diagnosed. POAG was the leading subtype as already in study A, with an even higher prevalence of 70.4%. Secondary glaucoma was found in 18.5% and PEX in 11.1%. By the nature of the study (only people with ICT above 21 mmHg included), no NTG was detected. 17.9% of all were considered glaucoma suspicious and one person was already declared a suspect.

Of those with the diagnosis of glaucoma, 59.3% were male, mean age was 53 years and 44.4% belonged to age group 4 (60-79 years). 44.5% presented unilaterally blind (33.3% in the right eye, 66.6% in the left eye). One person (3.7%) in the sample was bilaterally blind. All POAG cases will be analysed separately in the next chapter 3.4 as mentioned before.

3.3.3 Comparison between gender and different age groups

The unintended almost equal proportion between 52 male and 54 female participants (49:51 ratio) allows a comparison of results. Female median age was 39 years (mean 44.1; range 20-79), and male age was higher with a median of 48 years (mean 49.2; range 19-81). Of all females, 51.9% were over 40 years. Males over 40 represented 65.4%. Women were strongly present in the younger age group 2 between 25 and 39 (37%), and none in group 5 of 80 years and older. Males dominated in group 4 between 60 and 79 (35%), and also 1.9% in the oldest group of 80 and above.
Median IOP was almost equal in both genders. Men had a median ICT/GAT of 25/24 mmHg (range 11-81) versus ICT/GAT in females of 24.5/23.5 mmHg (range 11-72). Mean and median CCT values did not vary much between genders, although males had a slightly thinner CCT median. Median CCT for male eyes was 525.5 μm. Women presented a median CCT of 530.5 μm. ACD and ACA means were almost equal in both genders as in study A. ACD mean in both eyes of males and females was 2.8 mm. ACA means for males were between 38 and 39°, and in females 37° to 38°, the same as in the healthy study sample.

The CDR median for males was 0.4 in both eyes and 0.35 in women. A marked gender discrepancy was found in the amount of people with CDR values of 0.8 or more in at least one eye. While 11.1% of women fell into this category, 26.9% of men had CDR of 0.8 or worse.

While bilateral cataract was present in 25.9% of females, in males it was detected in 30.8%. 20.4% of women were unilaterally blind (27.3% on the right, 72.7% on the left eye) and 1.9% bilaterally blind. In contrast, 23.1% of men were unilaterally blind (50% on the right and 50% on the left eye), and 5.8% presented with bilateral blindness.

There were more men diagnosed with glaucoma, but more women declared as suspects. 20.4% of women were diagnosed with glaucoma upon examination, primarily with POAG, and 22.2% were described as suspects. 1.9% was diseased with PEX and 1.9% with secondary glaucoma. In men, almost one third (30.8%) was diagnosed with glaucoma, mainly POAG (19.2%), as well as secondary glaucoma (7.7%), and 3.8% PEX. 13.5% were determined as glaucoma suspects.

Comparing features of younger and older sample populations in study C, below and above 40 years, demonstrated more differences than comparing gender. In total numbers there were more men in the group over 40 years (54.8%) than women (45.2%), whereas in the group younger 40 years there was a female preponderance with 59.1% against 40.9%.

IOPs did not differ much in both groups. Medians for both eyes combined of those under 40 years were 25/23.8 mmHg in ICT/GAT, and among those over 40 years it was 24.3/24 mmHg. CDR median was higher in the older age group, with 0.5, while in the
group below 40 years it was 0.3 for both eyes. The elderly had a higher incidence of CDRs of 0.8 or worse, which was 29% in those over 40 years versus 4.6% in the younger.

There were further distinct findings between age groups. Like in study A, older patients showed lower median CCT values. Median CCT of those older 40 years was 511.5 µm (range 439-635) while in those younger 40 years it was 535.5 µm (range 451-623). Mean ACDs in the older group was lower, with 2.7 mm versus 3.0 mm in the younger, which was almost equal to the healthy group (2.8 versus 3.0 mm). ACA means were between 35-37° in the older group and 39-43° in the younger group (in healthy 34-35° and 38-40°).

Cataracts affected the older age group more (46.8% bilaterally versus 2.3% in the younger group). Likewise, vision deteriorated with age. 9.1% of the younger 40 years group were unilaterally blind (50% right, 50% left eye) and none was bilaterally blind. In the age group over 40 years, 6.5% presented with bilateral and 30.7% with unilateral blindness (36.8% right, 63.2% left eye blindness).

A disparity appears in terms of new or known glaucoma diagnosis. Those above 40 were given a definitive glaucoma diagnosis (mainly POAG) in 32.3%, which was twice as often as in the younger group with 15.9%. Vice versa, those below 40 years of age were considered suspects three times as often as the elderly, with 30% versus 10%. Furthermore, all people with a known diagnose of glaucoma (n=14, including one known suspect) were over 40 years and none below.

To repeat the concluding words of study A and B, the findings gave an indication that higher IOP values and glaucoma are closely associated with age. In respect to gender, men were older on average, presenting with more advanced glaucomatous findings and diagnosed more often with glaucoma and. The statistical correlation of these parameters will be demonstrated in chapter 3.5.
3.3.4 Summary of study C

Study C examined individuals with increased ICT measurements at the OPD. In the sample of 106 people with a median age of 43 years, almost 60% were 40 years or older. With an almost 50:50 gender distribution, 25.5% (n=27) were newly diagnosed with glaucoma, and 12.3% (n=13) already had glaucoma diagnosed. POAG was the leading subtype with 70.4%. Among those diagnosed with glaucoma, the mean age was 53 years and 59.3% were males.

Total mean ICT/GAT for both eyes was 26.7/25.9 mmHg, and total ICT/GAT medians for both eyes were 24.5/24 mmHg. Total median CCT for both eyes was 527 µm respectively. Excavation of the optic disc had a median of 0.4 in both eyes (compared to 0.3 in the healthy sample of study A). A very high number (18.7%) showed CDRs of 0.8 or more. 50% among those were newly diagnosed with glaucoma. A marked gender discrepancy was found regarding CDR values of 0.8 or more in at least one eye in women with 11.1% and men 26.9%.

3.8% of people with visual impairment and blindness were bilaterally blind, mainly in the age group above 40 years. Concurrently with high median age, 28.3% showed bilateral cataract.

Patients above 40 years had a higher incidence of CDRs of 0.8 or worse. 4.6% in those below 40 years contrasts 29% in those over 40 years presenting with a CDR of 0.8 or worse. Likewise, the elderly were diagnosed twice as often with glaucoma as their younger counterparts (32.3% versus 15.9%). Vice versa, those below 40 years of age were considered suspects three times more frequently than the elderly (30 versus 10%). All people with a known diagnosis of glaucoma were older than 40 years. In respect to gender, men on average were older and showed advanced glaucomatous findings.
3.4 Characteristics of POAG patients from study A and C

With POAG as the main glaucoma type in Africa, the following chapter focuses on this type. All 22 patients newly diagnosed with POAG in study A and C are presented combined in the following chapter. Of these 22 POAG patients, three are from study A, found among an allegedly healthy study population, and 19 from the sample of increased IOP levels of study C. Those patients with a known history of glaucoma have been excluded, as it was not sure that the same definition of glaucoma was taken for diagnosis and also because they were partially under treatment, which could distort the numbers and figures. The detailed table of results throughout the following chapters are found in Table A 5 in the appendix 9.3.5.

3.4.1 Total number of POAG patients, gender ratio, age distribution, mean IOP, CDR, CCT, ACA, ACD, cataract and visual acuity

Among all 22 POAG patients the male gender outnumbered the female with 54.5 to 45.5%, while in the total sample of study A and C there was a slight dominance of the female gender. A brief summary of main findings are summarized in Table 8.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>No.</td>
<td>22</td>
</tr>
<tr>
<td>Gender distribution (male : female)</td>
<td>%</td>
<td>54.5 : 45.5</td>
</tr>
<tr>
<td>Age mean / median</td>
<td>Years</td>
<td>52 / 54</td>
</tr>
<tr>
<td>IOP (ICT/GAT) mean</td>
<td>mmHg</td>
<td>30.2 / 30.3</td>
</tr>
<tr>
<td>IOP (ICT/GAT) median</td>
<td>mmHg</td>
<td>27 / 26</td>
</tr>
<tr>
<td>CCT mean / median</td>
<td>µm</td>
<td>504.7 / 505</td>
</tr>
<tr>
<td>CDR mean / median</td>
<td></td>
<td>0.7 / 0.7</td>
</tr>
<tr>
<td>CDR &gt; 0.8 (at least one eye)</td>
<td>%</td>
<td>45.5</td>
</tr>
<tr>
<td>Cataract bilateral</td>
<td>%</td>
<td>45.5</td>
</tr>
<tr>
<td>Unilateral blindness</td>
<td>%</td>
<td>31.8</td>
</tr>
<tr>
<td>Blindness bilateral</td>
<td>%</td>
<td>4.5</td>
</tr>
</tbody>
</table>
The median age was 54 years (mean 52 years; range 20-78). The majority of 72.7% belonged to the group of 40 years and older, where 27.3% were 40-59 years (group 3), and almost half (45.5%) of all were 60-79 years old (group 4). There was none 80 years or older. The group younger than 40 years comprised mostly people from 25-39 years (18.2%; group 2), and only 9.1% were younger 25 (group 1), shown in Figure 7.

Figure 7: Age group distribution of POAG patients (%), n=22

Median ICT/GAT was 27/26 mmHg and total mean ICT/GAT 30.2/30.3 mmHg (range 18-69 mmHg). These medians were above the average of study C, in which total medians were 24.5/24 mmHg with ICT/GAT.

Median CDRs among POAG patients were increased with 0.7 in both eyes, and 45.5% were detected at a very advanced stage with 0.8 or worse. Total median CCT was 505 µm and thereby was thinner in POAG patients than in the healthy population (507.5 µm). Mean CCT in all 22 POAG patients was 516.2 µm, but these included three patients with IOP values above 40 mmHg and one immeasurable IOP. Excluding these four from the calculation, because of their extreme IOP and thereby most likely thickened CCT values, results in a mean CCT of 504.7 µm, which is shown in Table 8, be-
cause this was regarded as the more accurate value. The mean ACD of 2.75 mm and the mean ACA between 36° to 39° did not differ much from the healthy sample.

31.8% of all POAG affected patients showed unilateral blindness (28.6% in the right and 71.4% in the left eye), whereas 4.5% (n=1) presented with bilateral blindness (among the healthy sample, no one was bilaterally blind; in the increased IOP sample 3.8% were bilaterally blind). Bilateral cataract was present in 45.5% of POAG patients. Due to only incipient to medium stage cataracts present, glaucoma seemed to be the cause of blindness in these patients, given their large CDRs or very elevated IOP values.

3.4.2 Comparison between gender and different age groups

The following paragraphs describe similarities and differences between results for both genders, and in between age groups, mainly patients below and above 40 years of age. A gender comparison among POAG cases shows that out of ten women 70% were 40 years and older. Among twelve men 75% were 40 or older. Men had a higher median age (68 years) with 50% being over 60 years in comparison to women (48 years) with 30% above 60 years of age.

IOPs in ICT/GAT measurements were about equal between both genders. In total, results show a higher IOP median in men. Median ICT/GAT for men was 27.5/26.5 mmHg and for women 25.8/24.8 mmHg. Male POAG patients had thinner CCTs compared to females. Total median CCT for men was 494.5 µm (range 439-568) versus 509.3 µm 458-541) in women. CDR findings in men are higher than in women. Median CDR in both eyes of men were 0.8 (range 0.4-1.0). In women, median CDR was 0.7 (range 0.4-0.8). While in women 30% had 0.8 or worse, in men it was 58.3%.

Cataract was also more prevalent in men. Bilateral cataract was twice as common (30% versus 58.3%). Concurrently, male VA was less than female VA. Women with POAG had 20% unilateral blindness (all in the left eye) and no bilateral blindness. Twice as many men - 41.7% - were unilaterally blind (40% in the right and 60% in the left eye), and 8.3% (n=1) were bilaterally blind.

Comparing ages below and above 40, there were almost three times as many POAG patients detected with age over 40 (n=16) compared to those who were younger than 40
In those younger than 40, gender distribution was 50:50. In those over 40 female-male ratio was 44:56.

ICT/GAT IOPs did not vary much between the two age groups. The total median ICT/GAT in those younger than 40 was 27.5/25.5 mmHg, and 26.8/26.3 mmHg in those above 40 years. There was a difference between CCT values of under and over 40-year-old people, as in previous studies. Under 40 years, CCT mean/median was 530.5/529 µm, whereas over 40 years mean/median was 494.5/493 µm, which is again in accordance with the fact of physiological decrease in CCT with age.

Resembling the results of the previous gender comparison, median CDR findings were mildly higher in the age group over 40. Median CDR was 0.65 in those younger than 40 years and 0.73 in those above 40 years of age. Half of all over 40 years presented with CDR findings of 0.8 or worse, against 33.4% of those below 40 years of age. This discloses that advanced stages often develop with increasing age. No cataract was found among those aged below 40, while 62.5% above the age of 40 presented with bilateral cataract. Accordingly, VA was worse with increasing age.

Male participants had a higher median age and presented with worse ocular findings, showing more risk factors for the development of glaucoma, such as high IOP, worse CDR, and thinner CCTs. The same was true for the older age group. These findings need to be interpreted in the light of the age distribution of the whole sample B of 1,112 patients. The majority of participants (58.2%) were female and 41.8% male. At the same time, the male population was older with 48% above 39 years, against 42% of women. The fact of an older male sample and the correlation between the development of glaucoma with age may contribute to the predominance of males in terms of pathologic glaucomatous findings. Furthermore, the correlations shown in chapter 3.5 will also indicate aforementioned associations.
3.4.3 Summary of findings in POAG patients

In general, POAG patients presented with high median age and share in patients above 60 years of age. Ocular parameters showed the highest IOP medians, thinnest medians in CCTs, more advanced CDR findings as well as low VA in comparison to the healthy sample of study A and the sample of increased IOP of study C. In general terms, rather advanced glaucoma stages were detected among POAG patients.

The median age was 54 years (range 20-78). Male gender with 54.5% outnumbered the female gender (45.5%). The majority (72.7%) among POAG patients belonged to the group above 39 years. While both age groups (above and below 40 years) had comparable median IOP values of 26.3 mmHg and 25.5 mmHg respectively, the younger POAG patients with advanced glaucoma stages presented with a higher CCT median (530.5 µm) than their older counterparts (493 µm) and also than the healthy population sample of study A (507.5 µm).

Median ICT/GAT-values were 27/26 mmHg. Median CDR among POAG patients was 0.7 and 45.5% of cases were detected at an advanced stage with CDR of 0.8 or worse. Total mean CCT was 516.2 µm and total median CCT 505 µm. Bilateral cataract was present in 45.5% of POAG patients. VA was on average worse than in the previous studies and 4.5% (n=1) presented bilaterally blind.

A gender comparison pinpointed a male majority in terms of older age and more advanced glaucoma stages. As glaucoma development is closely associated with ageing, the fact of an older male sample may contribute to the dominance of males in terms of pathologic glaucomatous findings. Male median age was 68 years versus 48 years in women. Men also showed larger CDRs, lower VA findings, and had thinner CCT values (median 494.5 µm) than women (509.3 µm).

Comparing POAG patients of older and younger than 40 years of age showed a CCT median of the elderly of 493 µm, which was thinner than in those below 40 years, where median was 530.5 µm. Vision was also worse in the latter group. CDRs were slightly more advanced in the older age group. CDR median was 0.65 in those younger 40 years and 0.73 in those above 40 years of age.
3.5 Correlations of ocular parameters

In order to determine how different features of interest are associated, correlation analysis was done, using metric parameters, namely age, ICT, GAT, CCT, and CDR. Furthermore, correlations were calculated for the dichotomous variables gender and age with the diagnosis of glaucoma. Statistical correlations were measured for each study by coefficient of correlation. Because the metric parameters were not normally distributed, Spearman’s correlation coefficient (rho) was chosen. The correlation coefficient ranges from -1.0, indicating perfect negative relation to +1.0, indicating perfect positive relation. The closer results come towards zero, the less two parameters are correlated. As already outlined in chapter 2.3 correlation of -1.0 to -0.5 or 1.0 to 0.5 is considered a strong correlation, -0.5 to -0.3 or 0.3 to 0.5 moderate and between -0.3 and -0.1 or 0.1 to 0.3 it is weak, whereas values between -0.1 and 0.1 mean no correlation. The correlation has statistical significance (p) with a p-value of < 0.05.

3.5.1 Correlations in study A and B

In the healthy study sample A and taking the means of both eyes, there was a strong and significant correlation between ICT and GAT measurements (rho = 0.863, p = 0.000).

Moderate and significant correlation was found between ICT and CCT (rho = 0.35, p = 0.000).

A weak but significant correlation was detected between GAT and CCT (rho = 0.244, p = 0.000) as well as very weak between age and CDR (rho = 0.13, p = 0.067).

No associations were found between CCT and CDR (rho = -0.054), ICT/GAT and CDR (rho = 0.117/0.107), nor age and ICT (rho = 0.006) or age and CCT (rho = -0.071).

In study B in which only the age and ICT measurements of patients were recorded, there was also no correlation between age and IOP.

In retrospect the variable of glaucoma diagnosis was added to study B after examining the individuals with elevated IOPs. The dichotomous variables age and gender were then correlated with the variable of glaucoma diagnosis to see the possible associations. In the presentation of results gender and age comparisons were often made. The total
numbers suggested a tendency of glaucoma to occur more often at higher ages and more often in men.

For gender and glaucoma diagnosis the chi-squared test gave no significant result (p = 0.075). Thus, gender does not seem to be correlated to the development of glaucoma. In respect to age and glaucoma diagnosis the Pearson correlation showed a weak but significant correlation of age and the diagnosis of glaucoma (r = 0.112, p = 0.000). Therefore, age can be associated with the development of glaucoma and the fact of an older male sample may influence the results. These tests also confirm the information given in the introduction under 1.2.1 and 1.2.6.

3.5.2 Correlations in study C and POAG sample

Comparable associations were found in study C and the separate POAG sample, which is explained by the fact that the POAG sample is mainly a sub-entity of study C. The following refers to study C but also applies to the POAG sample.

Just like in study A, strong associations with high significance were found between ICT and GAT (rho = 0.785, p = 0.000) for the mean of both eyes together.

A moderate and significant correlation existed between age and CDR (rho = 0.314, p = 0.001).

A weak but not significant correlation was present between ICT and CDR (rho = 0.184, p = 0.061). A weak but significant correlation between GAT and CDR (rho = 0.283, p = 0.004).

There was a weak and significant negative correlation between age and CCT (rho = -0.282, p = 0.003), as well as CDR and CCT (rho = -0.223, p = 0.022). In comparison, age and ICT/GAT were not (rho = 0.1) or very weakly correlated (rho = 0.194, p = 0.05). No correlation is present between ICT and CCT (rho = 0.105) or GAT and CCT (rho = -0.043).

3.5.3 Summary of correlations

Looking at the metric variables throughout all studies, common and strong correlations were only found between ICT and GAT measurements. A weak positive correlation was
found in study A and C between age and CDR, indicating that higher age is associated with higher CDRs. In all studies no correlation could be seen between IOP measurements in ICT/GAT and age. Age and glaucoma were weakly but significantly correlated ($r = 0.112$, $p = 0.000$). Gender was not correlated with the diagnosis of glaucoma.

In contrast in all other variables no consistency was found among the studies regarding correlation. In study A there was a moderate association between ICT and CCT ($\rho=0.35$, $p = 0.000$), which was not correlated in study C ($\rho=0.105$). The association between CCT and IOP is a topic of discussion in literature and subject of discussion in chapter 4.4.

The strong correlation between ICT with GAT will be further examined in the next chapter.

### 3.6 ICT and GAT comparison in Bland-Altman-plots

Complementary to the preceding descriptive statistics of results, the two methods for IOP assessment – ICT and GAT – are compared to each other in the following chapter. The statistical methods used are Bland-Altman-plots, done for right and left eyes of study A and B separately.

The Bland-Altman-plots are scatter diagrams, displaying means of paired values from each method on the x-axis, and mean differences of each pair of the two measurements for each individual on the y-axis. Three horizontal lines are added. The medial line represents the bias, calculated as the mean (overall) difference in values obtained with two different methods of measurement, namely ICT and GAT. As the plotted results display ICT minus GAT method values, the bias quantifies how much higher (positive bias) or lower (negative bias) values are with ICT.

The upper and lower horizontal lines represent the limits of agreement, in other words the confidence limit for the bias or degree of the average deviation of measured values. These limits are computed as bias (mean difference) plus and minus 1.96 SD of difference, resulting in upper and lower limits of agreement. The confidence limit is between upper and lower limits of agreement. The limit indicates the range within which 95% of
the differences from the bias are expected to be, if differences between the methods were distributed normally.

Figure 8 and Figure 9 depict Bland-Altman-plots for right and left eyes of study A. A very wide distribution of scatter points can be seen in Figure 8 for the right eye, whereas in the left eye, depicted in Figure 9, points are clustered more narrowly.

The 95% confidence limit of the right eye is from -3.09 to +5.57 mmHg, with a positive systemic bias or average difference of +1.24 mmHg, indicating that ICT measures on average about 1.2 mmHg higher than GAT. Evaluating the same for the left eye, it gives a confidence limit between -2.83 and +5.03 mmHg and a positive systemic bias of +1.1 mmHg.

The right eye of study A comprises nine outliers (9 of 191, 4.7%), eight above and one below the limits of agreement. For the left eye, the plot demonstrates ten outliers (10 of 188, 5.3%), five above and five below the limits. So in both eyes the two methods show a bias, which can be rounded to 1 mmHg overestimation of ICT compared to GAT.

Figure 8 : Bland-Altman-plot for study A, right eye (mmHg)
Figure 9: Bland-Altman-plot for study A, left eye (mmHg)

Figure 10: Bland-Altman-plot for study C, right eye (mmHg)
Figure 10 and Figure 11 illustrate Bland-Altman-plots for right and left eyes of study C, individuals who all presented with IOP values above 21 mmHg in at least one eye. Both plots show a rather wide distribution of scatter points. The 95% confidence limit of the right eye is wider than in study A, ranging from -5.58 to +6.62 mmHg. There is a positive systemic bias or average difference of +0.52 mmHg. This indicates that ICT-measures were on average about 0.6 mmHg higher than GAT-measures. Values in the left eye give an even wider confidence limit between -6.54 and +7.84 mmHg and a positive systemic bias of +0.65 mmHg.

For the right eye of study C, 7 of 105 (6.7%) outliers can be detected, four are above and three below the limits of agreement. For the left eye, the plot demonstrates 10 of 105 (9.5%) outliers, seven above and three below the limits. So in both eyes, like in study A, the two methods show a positive systemic bias of 0.5-0.7 mmHg. This is less bias than in study A, but with a higher percentage of outliers.

All have in common that the plots show a narrower scattering around the zero-point at lower IOP values. At higher pressure levels, distribution is wider and farther from zero. This indicates a larger difference between the two methods in higher pressure levels, suggesting that ICT is more inaccurate in measuring high IOP than in lower IOP ranges.
3.7 Summary of results

The most important results and findings are summarised below. Prevalence of increased IOP is summarized in Table 9. It shows that study A found 11.5% of increased IOP levels within an allegedly healthy, non-glaucomatous population. Two and a half percent were newly detected with glaucoma. Discounting these newly detected glaucomatous individuals among the healthy sample, the prevalence of increased IOP was 9.5% for healthy, Malawian eyes.

By screening with an ICT at the OPD of this hospital (study B), 13.8% were detected with raised IOP levels. Not all these could be further examined, but of those found with increased IOP who did get examined (study C), 2.4% were hence diagnosed with glaucoma.

<table>
<thead>
<tr>
<th>Study</th>
<th>IOP &gt;21 mmHg (%)</th>
<th>New glaucoma diagnosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study A, “Healthy” sample, including glaucomatous cases</td>
<td>11.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Sample A, excluding glaucomatous cases</td>
<td>9.5</td>
<td>-</td>
</tr>
<tr>
<td>Study B, Intraocular pressure assessment</td>
<td>13.8</td>
<td>2.4</td>
</tr>
</tbody>
</table>

The following Table 10 is a summary of results of studies A, B, and C regarding the prevalence of glaucoma and subtypes. The table shows the percentage of people newly diagnosed with any type of glaucoma during the study period and the percentage of glaucoma among all people with increased IOPs. It further gives a subdivision of the different glaucoma types that were detected.

One finding is the difference of glaucoma detection comparing study A, B and C. In the non-patient sample (study A) and the OPD sample (study B) the rate of glaucoma detection was 2.5 and 2.4%, compared to the sample with increased IOP patients (study C), where the number of new (excluding known glaucoma) diagnoses was 25.5%. Similarly, a focus on increased IOP levels in the samples of A and B led to detection of over 17% glaucoma cases. The main glaucoma type in Malawi according to results of this study is POAG with 60 to 70%.
Table 10: Prevalence of glaucoma and subtypes in current studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample number (n)</th>
<th>Newly diagnosed (%)</th>
<th>Newly diagnosed among increased IOP (%)</th>
<th>Glaucoma types (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (healthy sample)</td>
<td>200</td>
<td>2.5</td>
<td>17.4</td>
<td>POAG 60.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PEX 20.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NTG 20.0</td>
</tr>
<tr>
<td>B (IOP assessment)</td>
<td>1,112</td>
<td>2.4</td>
<td>17.5</td>
<td>-</td>
</tr>
<tr>
<td>C (increased IOP)</td>
<td>106</td>
<td>25.5</td>
<td>-</td>
<td>POAG 70.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PEX 11.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Secondary glaucoma 18.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NTG (excluded)</td>
</tr>
</tbody>
</table>

Abbreviations 1: IOP, intraocular pressure; POAG, primary open-angle glaucoma; PEX, pseudoexfoliating glaucoma; NTG, normal tension glaucoma

In general, mean and median CCTs in all samples were found to be low, indicating thin CCT findings among a Malawian population sample. An exception to low CCTs was the result of study B (sample with increased IOP). CCT findings and their implications form a major part of the discussion in chapter 4.4. POAG patients had high median age and IOPs, thin corneas, advanced CDR values, a high rate of cataract, and lower VA than their non-glaucomatous counterparts.

Male patients, especially those above the age of 40 years and elderly patients in general presented with more advanced glaucoma stages than their female or younger counterparts. These findings need to be interpreted in the light of the age distribution where males also showed a higher median age. This was confirmed by the weak but significant correlation between age and glaucoma. Gender and the diagnosis of glaucoma were not correlated. Further, mainly weak associations were found. The exception was a strong correlation between ICT and GAT and moderate correlations between IOP (ICT or GAT) and CCT, as well as between CDR and age.

A comparison between the two IOP measurement techniques ICT and GAT in Bland-Altman-plots have shown an overestimation of approximately 1 mmHg of ICT against GAT-values in the healthy sample. In the sample with increased IOP values, ICT overestimation was 0.5 to 0.7 mmHg. Implications of this finding on possible ICT cut-off points are discussed in chapter 4.5.1.
4 Discussion

The thesis has given an introduction to central topics of interest for this study, presented study designs, results and their statistical analysis. Following is a discussion of study results in perspective of prevailing opinions and data of the scientific world. A focus is put on studies from the African continent in order to have comparable samples and settings.

Chapter 4.1 compares the generated baseline data of a Malawian healthy, non-glaucomatous sample to values from other populations. Chapter 4.2 compares the prevalence of increased IOP levels and glaucoma in our studies to the prevalence in other countries. Chapter 4.3 describes glaucoma presentation patterns and is concerned with glaucomatous Malawian eyes, especially POAG characteristics, in comparison with findings in literature. The successive chapter 4.4 is dedicated to the discourse on CCT with related implications on IOP measurement outcomes, and the role as independent risk factor for development of glaucoma, as seen in the results of this and in comparable studies.

One central question of the present thesis is the usefulness of a screening programme at LSFEH and other African or development country settings. Therefore, chapter 4.5 deals with this question in accordance with recommendations from literature.

The last two chapters concentrate on the collected data in the context of Malawi, discussing the usefulness of an ICT screening for glaucoma. Firstly in chapter 4.6, all findings are discussed in the light of realities at LSFEH with a guideline proposal. Secondly, chapter 4.7 deals with the limitations of the study and data collection.

4.1 Comparative study of results for non-glaucomatous eyes

Table 4 in chapter 3.1.1 summarises main findings of “healthy”, non-glaucomatous Malawian eyes. These parameters serve as a baseline of ocular features in this population. In Hohmann’s thesis conducted in the same eye hospital, the group of patients with IOP below 16 mmHg (group I) and the group between 16 to 23 mmHg (group II), may
correspond best with the non-glaucomatous, “healthy” sample of this thesis. Her total sample comprised patients at LSFEH including 18% glaucomatous and the remaining non-glaucomatous eyes. Mean ICT of group I was 13.7 and group II 19.1 mmHg. Group I had a mean CCT of 509.83 µm, group II mean CCT was 516.9 µm, and in total CCT average was 513.52 +/- 36.22 µm. (Hohmann 2011) In general, her findings correspond to the present results of this study with 509.2 µm as a mean CCT. Both studies from the same setting give a clear indication of very thin CCTs at this setting in comparison to data from other researches from Africa and other regions.

Mohamed et al. conducted a comparable hospital-based cross-sectional study in Sudan. Their sample excluded POAG, corneal ectasia such as keratoconus, or any other corneal disease. They also excluded patients who had undergone any kind of surgery with corneal incision, and patients with history of ocular trauma. Their sample can be referred to as “healthy”, non-glaucomatous and thus be compared to our findings. In the Sudanese setting, mean CCT was 530.2 µm. (Mohamed et al. 2009) The Barbados Eye Study mentions remarkably thin CCT values of 529.8 µm among Barbados black participants. (Nemesure et al. 2003) Table 11 gives an overview of literature cited in Mohamed et al.’s article, for comparison of values from different populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Race</th>
<th>Mean CCT (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoffmann et al.</td>
<td>2013</td>
<td>German</td>
<td>552.2</td>
</tr>
<tr>
<td>La Rosa et al.</td>
<td>2001</td>
<td>African American</td>
<td>531.0-530.0</td>
</tr>
<tr>
<td>Mohamed et al.</td>
<td>2009</td>
<td>Sudanese</td>
<td>530.2</td>
</tr>
<tr>
<td>Nemesure et al.</td>
<td>2003</td>
<td>Barbados Black</td>
<td>529.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mixed Black/White</td>
<td>537.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>White</td>
<td>545.2</td>
</tr>
<tr>
<td>Wong et al.</td>
<td>2002</td>
<td>Chinese</td>
<td>555.1</td>
</tr>
<tr>
<td>Hohmann</td>
<td>2011</td>
<td>Malawian</td>
<td>513.5</td>
</tr>
<tr>
<td><strong>Present study</strong></td>
<td>2014</td>
<td>Malawian</td>
<td><strong>509.2</strong></td>
</tr>
</tbody>
</table>

It is apparent throughout the literature, that black populations show lower CCT values in comparison to other populations. Yet, since measurement techniques, instruments, as well as examiners vary among studies, values are not entirely comparable. Nevertheless,
thin CCT is a risk factor for glaucoma development and therefore these findings can raise awareness about populations potentially at risk, as discussed in chapter 4.5.3. The comparison of CCT means from different populations shows highest values in Chinese and Germans, and thinnest in Sudanese. By far the lowest CCT findings are the ones found in the present thesis. Since the measurements were taken by using the ASOCT and Hohmann came to similar findings using SP-100 Handy Pachymeter, the results can be considered to be very valid. They are extreme findings which suggest further research. Yet, referring back to the statement of Daughty and Zaman in chapter 1.2.6, CCT values between 503 to 565 µm could still be considered normal. (Doughty & Zaman 2000) Accordingly, Malawians would rank at the lower border of the normal CCT range.

4.2 Prevalence and implications of increased IOP

“Increased IOP”, as defined in chapter 2.2, were pressure values above 21 mmHg in at least one eye. In this case, findings were based on ICT measurements. As summarized in Table 9 of chapter 3.7, 11.5% of increased ICT values were recorded in the “healthy” sample (including ten glaucoma cases). Excluding those individuals results in a prevalence of 9.5% elevated IOP levels among a non-glaucomatous population sample. As there is no comparable literature about elevated IOP prevalence in the Malawian population, data from other regions is used for discussion of the findings.

A cross-sectional study among patients of a general practice, in a semi-rural district in South-Africa, assessed IOP using a Schiötz tonometer in 110 patients (87.3% white, 10.9% black). Aim of this study by van Niekerk et al. was to investigate the prevalence of increased IOP (above 21 mmHg) in a general practice. Findings indicate whether tonometric measurements of IOP, as one diagnostic option for glaucoma, should be performed by the general practitioner during routine examination. Further, the study tried to detect associations between increased IOP and possible risk factors. They detected increased IOP in 10% of the study sample (n=11 of 110). While among females in the general practice the prevalence of increased IOP levels was 7.3%, in men it was 17.9%. (van Niekerk et al. 2006) The study does not give any information about the age
distribution in males in females, which might be an explanation for the different prevalence of increased IOP levels.

A gender discrepancy towards the male can also be confirmed in the findings of studies A and B of the present thesis. In the non-glaucomatous sample (study A), increased IOP was present in 11.3% of “healthy” females compared to 11.7% of men. More obviously, during IOP assessment at the OPD (study B), 11.1% of females versus 17.6% of males had increased IOP levels. This was most likely due to the different age distribution between the genders with females being younger than males.

Comparing van Niekerk et al.’s data to the present research, the result of approximately 10% is in accordance with the present study data of the healthy sample. Therefore, a 10% prevalence of increased IOP among apparently healthy populations in this African region is regarded as appropriate. Among ophthalmologic patients, slightly higher prevalence rates between 11 to 18% seem to be a realistic approximation. These percentages are based on the present findings. In study B, among OPD patients, the total prevalence of increased IOP was 13.8%, which is higher than in the unaffected sample of study A. These prevalence findings from Malawi may be used as a basis for further discussions or consecutive researches and may help in clinical planning.

### 4.3 Glaucoma presentation patterns

The previous chapters described ocular findings and characteristics of “healthy” Malawians without a history of glaucoma to generate a baseline data set for this particular population. The subsequent chapters are concerned with glaucomatous Malawian eyes. Study findings will be compared with data from literature.

#### 4.3.1 Glaucoma prevalence and types

Table 10 in chapter 3.7 combines the results of studies A, B, and C regarding the percentage of people newly diagnosed with any type of glaucoma and the different glaucoma types detected. The prevalence of newly diagnosed glaucoma patients was 2.5% in study A, 2.4% at the OPD (study B) and 25.5% among those with increased pressure (study C). The mean age of those 27 new glaucoma patients was 53 years. Results of
present studies from Malawi indicate a glaucoma prevalence of 2.5% and POAG in 1.5% in the healthy sample. This is one of major study findings, since it shows glaucoma prevalence among a healthy Malawian sample and may give an approximation towards glaucoma prevalence in the Malawian population.

Yet as mentioned in the introduction on glaucoma prevalence, most prevalence data is given in respect to age. In Africa the number was 4.79% in people aged 40 to 80. In this study, the prevalence of glaucoma above 40 years was 4.6%, which is in accordance with abovementioned numbers.

The main glaucoma type in Malawi according to study findings of this thesis is POAG with 60 to over 70%. This finding is in accordance with numbers from other African countries, visualized in Table 12.

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Number</th>
<th>Glaucoma types (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Budenz et al. 2013)</td>
<td>Ghana</td>
<td>5603</td>
<td>POAG 94.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Secondary glaucoma 3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ACG 2.5</td>
</tr>
<tr>
<td>(Giorgis et al. 2012)</td>
<td>Ethiopia</td>
<td>602</td>
<td>POAG 37.7</td>
</tr>
<tr>
<td>(Gyasi et al. 2010)</td>
<td>Ghana</td>
<td>446</td>
<td>POAG 77.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NTG 8.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>POAG+NTG 1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Secondary glaucoma 1.7</td>
</tr>
</tbody>
</table>

Abbreviations: POAG, primary open-angle glaucoma; PEX, pseudoexfoliating glaucoma; NTG, normal tension glaucoma; ACG, angle-closure glaucoma

As mentioned in the introductory section 1.2.1, prevalence of glaucoma varies among regions. Glaucoma, especially POAG, is found most prevalent in Africa, with 4.79% of glaucoma (range 2.63-8.03) and 4.2% of POAG. (Tham et al. 2014) Ghana’s glaucoma prevalence numbers seem to rank among the highest in the world. 8.5% of people 40
years and older were affected as reported by Gyasi et al. and 6% according to Budenz et al. (Gyasi et al. 2010) (Budenz et al. 2013)

Kyari et al. claim the high prevalence numbers of glaucoma in Ghana to be an overestimation, after comparing different prevalence studies in SSA with rather varying percentages. This variance results from different glaucoma definitions and diagnostic criteria used by different authors. (Kyari et al. 2013) The challenge of non-uniform definitions is further discussed in chapter 4.7.

It has to be added to the discussion about increased glaucoma cases that ageing may primarily contribute to this upsurge. Yet, raised awareness through international campaigns and discussions as well as research and publications, has triggered an intensified effort to detect more glaucoma cases. Thus, whenever a disease is particularly screened or looked for, its numbers automatically rise. This is due to a higher detection rate, including false positives.

Regardless of the prevalence, glaucoma is the second most frequent cause of blindness in Malawi. (Kayange et al. 2014) (Kalua et al. 2011) Due to the deep impact on individual and national levels, detection of affected people is of utter importance.

4.3.2 Characteristics of eyes with POAG

The following discourse puts the findings about POAG patients of this thesis in relation to literature data. Focus will be on IOP, CDR, blindness, and cataract among POAG-affected individuals. CCT is separately dealt with in chapter 4.4. IOP, CDR and blindness values in comparison are visualised in Table 13.
Kayange et al. in their study on 60 POAG patients at LSFEH in 2010, found a mean IOP (GAT) of 35.5 mmHg in comparison to a mean IOP (GAT) of 30.3 mmHg in the present study. Furthermore, the majority of patients in their research showed severely cupped optic discs with 77% (n=46) having a CDR of 0.8 or worse. This number is in contrast to 45.5% in POAG patients of the present study. 15% of POAG patients in Kayange et al.’s study suffered from bilateral blindness, which is three times more than the present results of 4.5%. The reason for this discrepancy may lie in the nature of their study. Chronic POAG patients were recruited, of which the majority presented a year after onset of visual symptoms, whereas in the present study there were several subjects who did not have visual problems upon time of detection and three healthy individuals. (Kayange et al. 2014)

Giorgis et al.’s Ethiopian hospital-based prospective review of 602 open-angle glaucoma patients from 2009 presents very similar IOP results to POAG patients of the present study, but a higher incidence of advanced CDR stages, as shown in Table 13. (Giorgis et al. 2012)

Gyasi et al.’s data originate from a review of clinical records of all first-time attendants newly diagnosed with any type of glaucoma (mostly POAG) at a hospital in Ghana between 2003 and 2005. Mean IOP (GAT) was higher than in the present study and Kayange et al.’s results from Malawi, and more patients presented with bilateral blind-
ness (34.1%). Gyasi ascribes advanced glaucoma stages, including the high incidence of blindness from glaucoma firstly to the more aggressive nature of the pathology especially in black people. Secondly, he explains it with a late presentation to hospitals due to lack of awareness and education. And thirdly poor access to care as well as lack and inadequate distribution of ophthalmologists who are trained in trabeculectomies is mentioned as further reasons for advanced stages. (Gyasi et al. 2010)

It is worth recalling the painless nature of glaucoma, resulting in unawareness of the disease. As pain is the “driving force in seeking medical help” (Lawan 2013) glaucoma is not likely to motivate people to see a doctor. This statement is also supported by other reviewed literature (e.g. (Lawan 2013) (Kyari et al. 2013)). Painlessness results in presenting at very advanced stages in Africa and other parts of the developing world, often with largely cupped optic discs, loss of vision in one or both eyes or both phenomena combined. These features were partly also seen throughout the present study data.

One last characteristic aspect of POAG patients is the presence of cataract. As explained in chapter 3 during presentation of results, incipient to medium cataract was present in a high number of patients of study C and of POAG patients. In study C, 28.3% had bilateral cataract, of which 40% were diagnosed with glaucoma, 23.3% were known glaucoma patients, and another 10% were new or known glaucoma suspect. Of all glaucoma cases 48% had bilateral cataract, and of POAG cases 45.5% presented with bilateral cataract. In respect to cataract, Kyari et al. make an important statement. They suggest that in areas with high numbers of cataract, glaucoma prevalence and blindness are underestimated. Cataract is an easily visible diagnosis, but often optic discs are obscured by cataract lenses. Consequently, a definitive diagnose of glaucoma cannot be given. (Kyari et al. 2013) In the studies of this thesis, cataract was always incipient, which enabled to make a definite diagnosis.

As both diseases are associated with age, it is very likely that both occur together, which has implications on screening, as discussed in chapter 4.5.3. Correspondingly, mean age of all POAG patients with cataract (mean 63 years, median 65 years) was higher than
the POAG average (mean 52 years, median 54 years). The high coincidence of cataract and glaucoma is most likely due to ageing.

4.3.3 Gender and age characteristics in glaucoma presentation

In all three samples of the present research more women were registered (female/male percentages: study A 53% : 47%; study B 58.2% : 41.8%; study C 50.9% : 49.1%. Males had a higher median age and had higher glaucoma prevalence. Since the results in chapter 3.5 showed a weak but significant correlation between age and the diagnosis of glaucoma ($r = 0.112$, $p = 0.000$), it can be postulated that the higher age of the male study population can be partly an explanation for the higher incidence of glaucoma among men in these studies. In study A and C, a moderate correlation also existed between age and CDR (study A: $\rho = 0.13$, $p = 0.067$, study C: $\rho = 0.314$, $p = 0.001$).

In addition, no correlation was found between gender and glaucoma. Likewise, the Ethiopian study from the previous chapter also showed no statistically significant association between glaucoma stage and gender. (Giorgis et al. 2012)

Male preponderance is found in a lot of African literature. For instance, in Kayange et al.’s hospital-based survey at LSFEH among newly diagnosed POAG patients, there were three quarters male (73.3%), resulting in a male-female-ratio of 2.75:1. He further sees this finding in accordance with other African literature from eye hospitals in Nigeria, Ghana, and Tanzania, where males made up 74%, 65%, and 72% of POAG patients. (Kayange et al 2014) (Lawan 2007) (Mafwiri et al. 2005) (Gyasi et al. 2010)

Social factors may also be relevant in explaining the gender presentation patterns, as elderly females are more likely to stay at home, and are often financially dependent and worse off than men in terms of money. Also mobility, education, and thus the understanding of the importance to come for follow-up visits are lower in many women. Kayange et al. name socio-economic and cultural reasons as barriers for women, which result in lower health care attendance. A review of SSA-literature on glaucoma found no consistent association between gender and age. Nevertheless, five out of nine surveys showed higher male prevalence in POAG and also a higher likelihood for men to develop secondary glaucoma, e.g. following trauma. (Kyari et al. 2013) This imbalance
should be tackled by intervention programmes concerning glaucoma and most possibly any other health issue. (Kayange et al. 2014)

Regarding gender, a Ghanaian population-based study of adults of 40 years and older reports a higher number of males than females with glaucoma and POAG throughout all age groups, with a male-female-ratio of 1.5:1. They further cite a number of previous studies which all come to the conclusion of a higher prevalence of glaucoma in men than in women in Africa, Europe, and Asia with male-female ratios between 1.2 and 1.8:1. (Budenz et al. 2013)

Whereas in the present studies males presented with higher age and worse vision and higher prevalence of blindness (uni-, and bilateral), Courtright et al. present a contrasting gender-ratio regarding blindness in Malawi. In their examination, blindness was more common in women and the male-female ratio for bilateral blindness was 1:1.94. (Courtright 2003) Further contrasting findings to results of this thesis are from a hospital-based study in Nigeria dealing with the economic burden of POAG for patients. Glaucoma was seen more often in females, although according to the authors of the study, there is no general gender predilection in POAG. (Adio & Onua 2012)

Quigley and Broman in their data review on the prevalence of glaucoma worldwide, also come to contrary conclusions compared to the present study. They predicted in 2006 that on a global scale, women will comprise 55% of POAG, 70% of ACG, and 59% of all glaucoma in 2010, and thus women are disproportionately affected. The main explanation of the high female prevalence among ACG, especially in Asia, was their relatively longer life expectancy. They advise a focus on female gender in eye care services, because women were estimated to develop B/VI twice as often compared to men and therefore need special attention. (Quigley & Broman 2006) (Resnikoff, S. et al. 2004)

Conclusively, on the global scale, no clear indication can be given as to which gender is affected more by glaucoma. Also in the present studies from Malawi, no gender correlation to glaucoma can be seen.

There are diverging findings when comparing the age of POAG patients. The group younger than 40 years presents with less advanced ocular findings and glaucoma stages,
thicker CCTs, better vision and no cataract. IOP values did not differ much between ages above or below 40 years (see chapter 3 for details). In general, analysis of the findings gives clear indications of glaucoma being a disease closely associated with age, as more people in the age group of 40 and above were newly diagnosed with glaucoma. For instance, in study C, no person below the age of 40 was found with a known diagnosis. Therefore all were 40 years or older. Ntim-Amponsah et al. even found an exponential trend line to correctly represent the prevalence of glaucoma with age in Ghana. (Ntim-Amponsah et al. 2004)

Nevertheless, more than a quarter (27.3%) of all newly diagnosed with POAG throughout our studies was younger than 40 years. In detail, these younger patients included 9.1% (n=2) between 18 and 24 years, and 18.2% (n=4) between 25 and 39. These young individuals partly had very advanced glaucoma, e.g. the 21-year-old man, unilaterally blind and excavations of 1.0 and 0.9, or a 20 year old women with 0.7 and 0.8 cupping as well as a 27 year old woman with CDR of 0.6 and 0.7, who both attended the clinic because of itchy eyes, and all three became part of the study due to their ICT readings of minimum 28 mmHg.

Tham et al. analysed the effect of age on POAG prevalence and found varying odds ratios (OR) across different regions. Despite the fact that POAG prevalence was highest in people of African ancestry at all ages, a steeper increase with age per decade was found in Hispanics and patients with European ancestry. (Tham et al. 2014) This finding supports the suggestion that in Africa, glaucoma detection should focus on age, as by nature it is a disease of age. It could be useful, though, to also target younger ages, as among Africans it occurs more often in young people than in other populations.

This finding is also underlined by Ntim-Amponsah et al.’s observations from Ghana, in which they stress that the onset of the disease is earlier and more aggressive in Africans than in Caucasians. The overall glaucoma prevalence in the population was 8.4% (8.2% in females, 8.6% in males). In the age group 30 to 64 years prevalence was 6.6% compared to 16.4% above 65 years. This proves a high association of glaucoma with age. Nevertheless, it is noteworthy that a prevalence of 6 to 7% in the young age group of 30 to 39 years is already high. (Ntim-Amponsah et al. 2005)
Not only is age a risk factor itself for the development of glaucoma, but also for blindness from the disease. As an example in Kyari’s study, more elderly people were found blind, and the average age of blind glaucoma participants was 74.8 years in comparison to 65.4 years of the seeing participants. (Kyari et al. 2013) In the same line, a Ghanaian study reports that people of 60 years and older are twice as likely to present to the hospital with advanced glaucoma stages, compared to younger ones. (Ntim-Amponsah et al. 2004) A finding, which is in accordance with our study results, having implications on screening programmes, as discussed in chapter 4.5.

4.4 CCT, its influence on glaucoma development and diagnostics

This chapter is dedicated to the discussion on CCT and its implications on glaucoma development and diagnostics, especially with applanation tonometry. The low CCT findings in the present studies and special role in the development and detection of glaucoma justify a separate chapter on this topic.

4.4.1 CCT findings in comparison

As already described in the introductory chapter 1.2.6, Hohmann detected one of the lowest CCT-measurements among people of African descent. (Hohmann 2011) Table 14 gives an overview of findings from different studies for comparison.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Non-/Glaucoma</th>
<th>Race</th>
<th>Mean CCT(µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aghaian et al.</td>
<td>2004</td>
<td>75% Glaucoma</td>
<td>US (all)</td>
<td>542.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>African Americans</td>
<td>521.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Japanese</td>
<td>531.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chinese</td>
<td>555.6</td>
</tr>
<tr>
<td>Hohmann</td>
<td>2011</td>
<td>Non-glaucoma</td>
<td>German</td>
<td>561.95</td>
</tr>
<tr>
<td>Hohmann</td>
<td>2011</td>
<td>18% Glaucoma</td>
<td>Malawian</td>
<td>513.5</td>
</tr>
<tr>
<td>Present study</td>
<td>2014</td>
<td>Glaucoma (POAG)</td>
<td>Malawian</td>
<td>504.7</td>
</tr>
<tr>
<td>Present study</td>
<td>2014</td>
<td>Non-glaucoma</td>
<td>Malawian</td>
<td>509.2</td>
</tr>
</tbody>
</table>
In order to put CCT results of this study in a global context, Aghaian et al.’s retrospective study is taken for comparison. They evaluated CCT measurements by ultrasound pachymetry in Asian, Caucasian, Hispanic, and African American patients in a US glaucoma practice, including 600 glaucomatous and 201 non-glaucomatous eyes. Therefore, values do not represent glaucomatous eyes only, but are a rough orientation as 75% of the sample is from glaucoma patients. Mean CCT in the US glaucoma practice was 542.9 µm. African Americans presented with the thinnest CCT (521 µm), while all other groups were above, ranging between 531.7 (Japanese) and 555.6 µm (Chinese). In the subdivision into ethnic groups, the trend towards a comparatively thin CCT in Malawians, and most likely Africans in general, is obvious.

Hohmann’s Malawian sample with 18% glaucomatous and the remaining non-glaucomatous eyes presented with an average of 513.5 µm, minimum of 431 µm and maximum of 595 µm. She divided all patients into three groups according to their IOP. In group I of her sample with IOPs below 16 mmHg, mean CCT was 509.83 µm. This group may correspond most with the non-glaucomatous, “healthy” sample of this thesis. Hohmann’s German control group, mean CCT was markedly higher. (Hohmann 2011)

In the present studies of this thesis, CCT values were found to be equally low or lower than Hohmann’s values. Due to the extreme findings, the numbers are outlined again in the following. As CCT data did not have normal distribution, medians are indicated, but for better comparison with literature data, means are also given. It was already explained in the presentation of results in chapter 3.4 that mean CCT of all POAGs was 516.2 µm, including very extreme IOD values of over 40 mmHg and very oedematous CCTs. Therefore, the mean CCT value taken for comparison excluding these extremes (n=4), is indicated as 504.7 µm for POAG patients. In the healthy sample mean was 509.2 µm. Median for both eyes from POAG patients of 505 µm. In the healthy sample (study A), total median was 507.5 µm. CCT in the eyes of a healthy Malawian population sample ranged from a minimum of 423 µm to maximum 613 µm, and in POAG patients from 439 to 632 µm. Therefore, while Hohmann already claimed to have found the thinnest CCT values ever measured on the African continent, the present data underscores hers and shows even lower CCT findings for Malawians.
4.4.2 Causes of thin CCT findings

A first cause of thin corneal findings is the ethnic origin of patients. As already designated in the introduction on risk factors for glaucoma, (see chapter 1.2.6) Africans are known to have thinner corneas compared to people from other geographical descent, providing them with an innate potential risk factor. The abovementioned findings from present Malawian studies and from glaucoma patients of different ethnic origin in the US support this finding. The authors of the US study noticed that glaucoma suspects and glaucoma affected patients showed CCTs which were significantly thinner than in unaffected participants, especially in African Americans. (Aghaian et al. 2004) Also Nemesure et al. found thinnest corneas in black POAG patients from Barbados. (Nemesure et al. 2003)

The German Gutenberg Health study of almost 5000 subjects found CCT to be age dependent, as from 35 to 44 years of age CCTs were thicker than in subjects from 45 to 54 years. After 54 years, CCT was not decreasing further. (Hoffmann et al. 2013) Also Aghaian et al. found a relationship between thin corneas and increasing age. (Aghaian et al. 2004) Doughty and Zaman summarize in their literature review and meta-analysis that there was, indeed, a decrease of CCT with increasing age, especially after 60 years in non-CAUCASIANS (“non-whites”). In contrast, among Caucasians (“whites”) no apparent influence of age on CCT was found. (Doughty & Zaman 2000)

An age and pathology link with thin CCT values conforms to the present study data. The thinnest CCT values were found among POAG patients above 40 (median 493 µm). The age-pathology and thin cornea link is obvious when comparing this data to healthy people below 40 (509.5 µm), and most strikingly compared to POAG patients below 40 years (530.5 µm). Very low median CCTs were found among all POAG patients (505 µm), as well as among healthy participants above 40 (502 µm). Controversially in these findings, CCTs in healthy individuals below 40 years was thinner compared to glaucomatous, whereas thinner CCTs were expected not in healthy but in glaucoma patients. These findings may be explained by the presence of very high IOPs among glaucoma patients, which is discussed in chapter 4.4.3.
It is remarkable that within the same group, e.g. study A, people below and above 40 years differ in CCT medians - 509.5 versus 502 µm – which is a 7.5 µm difference between age groups. In comparison, in POAG patients the difference is larger. Median CCT in the younger group is 530.5 µm versus 493 µm, which gives 37.5 µm difference. These findings give rise to the question if the age related decrease of corneal thickness is a risk factor for developing glaucoma rather than the low CCT itself. This could then be taken into consideration in monitoring patients.

Thinnest corneas were documented among POAG patients above 40 (median 493 µm). Second thinnest corneas in the data were recorded in male POAG patients who included the majority of people above 40 (median 494.5 µm).

It has to be mentioned that a decrease of corneal thickness is a physiological development occurring with age and is not per se pathological. (Spoerl et al. 2009) Nonetheless, thin corneas stay an independent risk factor for glaucoma development, as described in chapter 1.2.6. Hence, thin CCTs and glaucoma occur especially at older ages, and “non-white” populations seem to be especially prone to it. As this research found extremely thin corneas, this fact should be taken into consideration in discussions and management of glaucoma in this setting. The next chapter also deals with the topic of thin CCTs and the implication for disease development.

4.4.3 Influence of thin CCT on the development of glaucoma

The association of increased IOP with the development of glaucoma is widely known and accepted as the most important risk factor for the development of the disease. (Boehm 2011) High IOP can be paralleled to thin CCT as it is said that the chance to develop optic nerve damage is 36% in untreated patients with IOP of 26 mmHg or above, as well as with CCT values of 555 µm or below. In contrast, if IOP is below 24 mmHg or CCT above 588 µm, the same risk is reduced to 2%. The OHTS – the first study finding this relationship between thin CCT and glaucoma progression - mentioned a threefold greater risk of developing glaucoma for eyes with CCT of 555 µm or less, compared to eyes with CCT of more than 588 µm. (Gordon & Beiser, J. et al. 2002) Also in the European Glaucoma Prevention Study, low CCT values were found to be a pow-
erful predictor for the development of POAG in patients with ocular hypertension (IOP 22 to 29 mmHg). (Gordon *et al.* 2007)

To refer back to the present study data, CCTs in all cases are far below the abovementioned 555 µm. IOP values in the POAG group surpassed the 26 mmHg in 77.3%. Thus, from both aspects (CCT and IOP values) the Malawian study population may have a high risk to develop optic nerve damage in the course of the disease, if not already present.

In those cases in which nerve damage has already taken place, the link between thin CCT and glaucoma progression can be hypothesised. In study A, those with high CDR of 0.8 or above show very thin CCTs (median 507 µm). Yet, CDR and CCT were not correlated.

In study C with IOPs above 21 mmHg, the group of CDR 0.8 or worse shows most remarkable CCT findings. The group is comprised of 50% newly diagnosed and 50% known glaucoma patients. Median for this group is 489.5 µm (mean 501.6 µm), which is the lowest of all study results, and is accompanied by 50% bilateral blindness in this group. There was a weak and significant negative correlation between age and CCT (rho = -0.282, p = 0.003), as well as CDR and CCT (rho = -0.223, p = 0.022). This negative correlation reflects the knowledge that a higher age and a large excavation are correlated with a thinner CCT. Ergo, thin CCT in line with high IOP can be confirmed as a risk factor for the development of glaucomatous damage to the optic nerve, with a high risk of blindness in the study population at LSFEH in Malawi.

### 4.4.4 Influence of thin CCT on IOP measurements

Many articles discuss the influence of CCT and further corneal parameters on IOP measurements. Especially since IOP control at certain individual target pressures is crucial for stopping the progress of the disease, accurate IOP determination is of utter importance. (Boehm 2011) (Neuburger 2011) (Rosentreter *et al.* 2011)

It is a controversy if IOP readings represent true IOPs of individuals, as these are only accessible by intracameral measurements. (Boehm 2011) A question is if IOP is really higher in people with thicker CCTs or if IOP readings in people with thick or thin CCTs
are over- or underestimated, which could be explained by physiology and mechanics of ocular applanation used to measure IOPs. Already Goldmann himself described that measurement errors are likely to occur in thin or thick corneas, due to the dependency of applanation on corneal composition. (Goldmann & Schmidt 1957) Different authors describe that more power is needed to applanate a thicker surface than the force necessary for a fine one. Thereby, on thick corneas, IOP is rather measured too high or overestimated, whereas in thin corneas, it is rather measured too low or underestimated. (Boehm 2011) (Doughty & Zaman 2000) (Hohmann 2011) (Neuburger et al. 2011)

Hohmann warns that this phenomenon may lead to mistaking people with thick corneas as ill due to high IOP levels, but leave others with thin corneas untreated because of falsely low IOP readings. This can result in missed opportunities for early glaucoma detection. Ignoring those with thin corneas may be most fatal, due to the more aggressive progress of glaucoma development and the higher risk of optic nerve damage, as illustrated above. (Hohmann 2011)

In her Malawian study, she uses a correction formula for ICT and GAT values, as she found significant influence of CCT on these parameters, needing correction. (Hohmann 2011) Many different corrective formulas exist, since GAT is designed for an average CCT of 520 µm and a lot of data does not correspond to this average. In the discussion of different nomograms, there is neither an agreement which is most adequate, nor if correction of measures is useful at all. In accordance with the current state of knowledge, a correction formula was not deemed appropriate or necessary and was therefore not considered in the presentation of results or the following discussion. Nevertheless, a short discourse follows on how CCT and IOP readings may possibly interact and be corrected.

A well-known table is Kohlhaas’s correction table for GAT. For every 25 µm deviation from 550 µm it corrects the measured IOP for 1 mmHg upwards (in thinner corneas) or downwards (in thicker corneas). Nevertheless, it is only valid for pachymetry-measured readings between 460 to 705 µm and was mainly designed from healthy eyes. Transferring them onto pathological eyes can be erroneous. (Neuburger et al. 2011) (Rosentreter et al. 2011)
Feltgen et al. found in a study, in which they actually compared applanation tonometer values with those of direct invasive intraocular measurements, that CCT had no relevant influence on applanation measurements. (Feltgen et al. 2001) Doughty and Zaman discuss that routine correction of tonometry results for CCT differences may not give clinicians more certainty in diagnosing or starting treatment of people with conspicuous findings. (Doughty & Zaman 2000) It is advised by Doughty and Zaman to use pachymetry on corneas of patient eyes with chronic disease, if IOP measurements show borderline or suspicious results. They claim, applanation tonometry is not significantly influenced by CCT of healthy eyes. (Doughty & Zaman 2000)

A trend of positive correlation between IOP and CCT is seen in the present studies. Higher IOPs were recorded together with higher CCT values. The healthy sample (study A), with only 11.5% IOP readings above 21 mmHg, had thinner mean (509.2 µm) and median (507.5 µm) CCT values than the sample with 100% IOP readings above 21 mmHg (study C), where mean CCT was 527.8 µm and median 527 µm. Thus, thicker CCT and higher IOP readings can be assumed to be related in this data, which is also explained in the following text. In terms of correlation, as mentioned in chapter 3.5, CCT and ICT/GAT were only moderately or weakly correlated (rho = 0.35, p = 0.000/rho = 0.244, p = 0.000) in study A, but not correlated in study C.

Mohamed et al. found a strong positive correlation between CCT and GAT IOP-readings with p<0.001, and therefore recommends routine CCT assessment in every patient attending a glaucoma practice. (Mohamed et al. 2009) Correspondingly Vijaya et al. state, that a 100 µm increase in CCT in their study was found to be associated with an increase in IOP of 1.96 mmHg in the rural, as well as 2.45 mmHg in the urban population. (Vijaya et al. 2010) Also Hoffmann et al., in a large German cohort study, found IOP to be positively correlated with CCT, when using non-contact tonometry, which was known and therefore expected to be positively correlated with CCT. (Hoffmann et al. 2013) Doughty and Zaman’s meta-analysis of CCT-IOP-associations exposed a statistically significant correlation between both parameters with a 10% difference in CCT resulting in 3.4+/-.9 mmHg difference in IOP (p<=0.001, r=0.419). Furthermore, they revealed differences between healthy and chronically diseased eyes. The cited 10% difference in CCT was smaller for healthy eyes (1.1+/-.6 mmHg, p=0.023, r=0.331),
but for eyes affected by chronic disease (POAG, ocular hypertension (OHT), NTG, diabetes, or lens exfoliation syndrome), IOP change for a 10% CCT difference was 2.5+/−1.1 mmHg (p=0.005, r=0.45). (Doughty & Zaman 2000)

According to Boehm, it would be most preferable to assess IOPs independent of CCT as far as possible, avoiding the need for CCT-correction formula altogether. (Boehm 2011) Also Ehrlich et al. suggest using cornea-independent IOP measurements. They used an Ocular Response Analyzer (ORA) which provides non-contact, CCT-independent IOP (corneal compensated IOP, IOPcc) in addition to the regular Goldmann-IOP (IOPg), and is able to measure corneal hysteresis (indicating tissue property by viscosity) and the total corneal resistance factor (CRF). (Boehm et al. 2011) Thereby they can compare IOPcc and IOPg for accuracy. In conclusion, for higher sensitivity, specificity, and for better identification of glaucomatous optic neuropathy (GON) they adjusted the GAT threshold to 20.9 mmHg and gave the abovementioned recommendation for CCT-independent IOP measurements. They focused on NTG, which presented with lowest CCTs and was thus most likely to lead to erroneous GAT measurements. (Ehrlich et al. 2012) Nonetheless, ORA measurements, especially for glaucoma patients, are under discussion. Since ORA cannot readily applanate the cornea in eyes with high pressure, values might be falsely low and must be interpreted with caution. (Neuburger et al. 2011)

In a setting such as LSFEH, a CCT-independent method, such as ORA, would be very gainful due to the present low CCT values. It is very unlikely to be realizable, though, mostly due to financial reasons. Whichever method is used to measure IOP, clinicians should take CCT as well as further corneal biomechanical properties which influence IOP measurements in consideration when managing glaucoma and ocular hypertensive patients. One option is to lower the target pressures of patients with thin CCTs, as also suggested for LSFEH in chapter 4.6. The reason for this was the likely underestimation of IOP in thin corneas. (Boehm 2011) (Hoffmann et al. 2013) Before proposing a guideline for glaucoma management at LSFEH in section 4.6, the next chapter will elaborate on glaucoma screening in the developing world.
4.5 Glaucoma screening in the developing world

One of the main objectives of this thesis is to evaluate the present data and draw conclusions regarding the relevance and design of a possible screening programme at LSFEH and comparable settings. The principal questions that will be answered throughout this chapter are which screening test(s) could be used (chapter 4.5.1), at which age and intervals screening should be implemented (chapter 4.5.2), and which target groups should be focused on (chapter 4.5.3). During the elaboration on possible screening tests, a focus will be placed on IOP assessment with ICT and possible IOP cut-offs. The final part of this chapter (4.5.4) points out the special role of non-ophthalmologists in the management of glaucoma.

4.5.1 Screening tests

In addition to the “Wilson criteria for screening” already outlined in the introductory chapter 1.2.7, a screening test in general, as well as for glaucoma, fulfils the following preconditions: (Mowatt et al. 2008)

- Proven to be safe
- Easy to handle, transport and understand
- Quick and well-tolerated by subjects
- Highly sensitive, specific and cost-effective

In the international community there is no consensus about which screening tests are specific and sensitive enough to be acceptable, as neither a single one nor group of tests is yet convincing enough to screen for glaucoma. (Cook 2009) (Mowatt et al. 2008) (Lawan 2013) Many suggestions are made regarding screening strategies, of which the most relevant are described below.

The first three abovementioned points can be approved for IOP screening by ICT measurements. Sensitivity and specificity are questionable. According to Hohmann, tonometry-based glaucoma-screening might be suitable for eye hospitals in developing countries, as it enables to detect and refer patients with highly elevated IOP levels, who possess a realistic risk of developing glaucoma. IOP assessment should be of major importance in an eye clinic in developing country settings. (Hohmann 2011) A major
challenge though, is the lack of ICT and GAT at eye departments and primary health centres, as well as sufficient staff trained to use them. As only few GATs are present in southern Malawi, which can be managed only by few staff members, many patients leave the eye clinic without receiving IOP-measurements.

Lawan affirms that IOP seems to be the easiest parameter to assess glaucoma. Furthermore he approves of IOP screening, since IOP is the parameter in glaucoma which is most responsive to treatment and thus worth detecting. Yet, if GAT is chosen, equipment and skills levels rise significantly compared to the mobile ICT. (Lawan 2013)

On the contrary, there are very depreciative opinions about tonometry as glaucoma screening tool. Wang et al. declared the handheld tonometer, despite their advantage of being easy to handle even by non-eye specialists, not worth their expense, as they are of no use in the detection of ocular disorders. (Wang et al. 1998) The AAO concludes according to their literature review, that IOP assessment is an ineffective glaucoma screening test for populations, because on the one hand too many POAG patients fall below the threshold of 21 mmHg and still develop glaucomatous damage. On the other hand, too many referrals with increased IOP levels never progress on to glaucoma. (AAO 2010b)

Results from the present studies can also not support the idea of IOP screening by ICT alone in a healthy population. By screening 200 healthy people (study A), only 2.5% in a basic population of apparently healthy individuals, and 2.4% at the OPD of LSFEH (study B) were eventually diagnosed with glaucoma after taking measurements from 1,112 people. Accordingly, the sensitivity of only ICT readings above 21 mmHg regarding the definitive glaucoma cases was 80% and specificity was 90%, with a PPV of only 17% and a NPV of 99.4%. These results demonstrate that the ICT method might partly be successful in identifying true healthy individuals amongst an entity but not very precise in exposing true ill people. Yet, as mentioned before, the differing sample size of glaucoma and non-glaucoma must be kept in mind, but also the fact that glaucoma is in reality only present in a small percentage of people. The low PPV is a strong indicator that an isolated ICT screening in the study population of Malawi. Thus by using only ICT, a very high number of people would need to be screened with only few detected
cases and would certainly miss out all those with NTG. A combination with another test might be useful, which will further on be elaborated.

Consequently, a recommendation for a general population-based ICT screening in Malawi or for all patients at LSFEH cannot be proposed. It would be too money- and staff-consuming in a country which has to tackle many other fundamental and more life-threatening challenges.

Wang et al. manifested already in 1998 in their study at a primary care centre with 94% black participants aged 40 or older, that no single test can be identified which reliably detects glaucoma cases. They recommend a **two-stage strategy**. Stage one consists of a questionnaire (asking for age, history of eye disease, history of diabetes, self-reported visual acuity, and new ocular symptoms) to detect patients at high risk, who can then be referred to specialist for further examination. For asymptomatic adults, the recommendation is a comprehensive eye examination every two years. The second stage is visual acuity testing and thorough fundus examination. Tonometry alone with IOP >21 mmHg in either eye had a sensitivity of 27% and specificity of 96%, detecting only 29% of glaucoma cases. Visual field testing had a sensitivity of 70% and specificity of 67%. The two-stage approach gave the best results. (Wang et al. 1998)

Comparably, the German BVA and DOG recommend screening for glaucoma by first assessing the history of risk factors, to then do stereoscopic assessment of papilla and peripapillary nerve fibre layer, followed by slit lamp examination of the anterior or medial segments of the eye and GAT. (BVA & DOG 2006)

**Questionnaire, VA plus ophthalmoscopy** combined together in Wang et al.’s study resulted in sensitivity levels of 83% and specificity of 76%. They come to the final conclusion that there is only one, if any, singular screening test able to filter out a good proportion of individuals affected by an eye disease with acceptable levels of specificity, namely ophthalmoscopy. It should be exerted by an experienced clinician on dilated pupils, to examine the optic disc and retina. They admit though, that an expert is not necessarily available at primary levels. Therefore, they suggest the alternative of digital fundus images, which could then be graded by trained personnel at a remote centre. (Wang et al. 1998)
Also Spry and Sparrow agree on the conclusion that no single test for glaucoma can convincingly discern affected from unaffected people. Rather a **two- or three-test combination** is needed. Most efficient is again a combination of optic nerve assessment plus visual field testing. Thirdly, IOP could be measured in order to help deciding to prioritise treatment among patients, due to an increased risk of people with high IOP levels to develop POAG. (Spry & Sparrow 2005)

These suggestions of test combinations aim for optimum disease detection under optimum conditions. In developing countries, as so often, ideals have to be set into the perspective of present conditions. First and foremost, the technical possibilities have to be judged realistically. For instance, in the present study, no perimetry was available. This is reality in many health care settings around the globe. (Bowman & Kirupanathan 2006) Expertise was given at LSFEH, but the density of trained ophthalmologic experts in the developing world is low, as mentioned in the introduction. Thus, idealistic screening suggestions are put into the light of developing countries.

Besides being specific and sensitive enough, another aim of screening tests is to detect a disease in its **early** stage. Early detection of glaucoma, though, proves difficult in general and especially in developing countries. (Friedman 2007) A realistic goal for the developing world would be to detect at least advanced glaucoma stages in patients who are most likely to otherwise go blind. (Rotchford 2005) Despite the risk to detect only advanced cases by screening in developing countries, positive side-effects may come along with any type of screening, which is the existence of the disease in general including education of signs and symptoms. (Mansberger 2010)

The ideal of early detection of glaucoma cases before the stage of optic nerve damage and symptoms of visual loss is worthwhile in the long run. For **developing countries**, it should realistically be altered to **medium to late cases**. Those are easier to detect, patients are more likely to present to clinics, and can still benefit from treatment. Furthermore, advanced technique and skills are desirable at any location, but a screening test in the developing world should first and foremost be **simple and easy** to administer. (Cook et al. 2009) (Hohmann 2011)
The fact of late presentation to the hospital can be used effectively in the detection of glaucoma, if more ophthalmological experts or health care workers are trained in fundus examination. At this specific setting, glaucoma patients were more likely to present with highly cupped discs than with visual symptoms. (Kayange et al. 2014)

Also in the findings of this thesis, many newly detected glaucoma cases did not show or complain of any visual symptoms, but had severely cupped optic discs. Thus, cupped discs should be the primary target of eye examinations. This was done in a study reported from Nigeria. An expert team screened for glaucoma suspects by first assessing CDRs of healthy subjects. IOP measures were only taken of those with suspiciously cupped discs or asymmetry between both eyes. Surprisingly, 97.8% of glaucoma suspects (according to their definition of suspects) had normal IOP values. (Pedro-Egbe & Waziri-Erameh 2010)

This leads to the conclusion, that ICT measurements of IOP miss out on many NTG cases or cases with normal IOPs at the time of examination plus giving many false positives and negatives. But the ICT technique fulfils the precondition of an easy and simple test, which is well tolerated by patients. On the other hand, fundus examination by an expert team is more likely to detect both NTG and POAG with increased IOP levels, as their main focus is optic disc damage, the strongest and safest sign for the presence of glaucoma. Slit-lamp funduscopy requires immobile and more expensive equipment, more expertise and time. These are unfavourable preconditions for a test to be applicable as screening tool in developing countries. Yet, a combination of ICT and funduscopy might be most useful in this setting.

Giving out questionnaires to filter people at high risk appears to be a simple way to do efficient referrals at first thought. Yet, in settings in which many people have never attended school, many are unaware of the type and concept of diseases which might run in their families or affect themselves, such as diabetes or glaucoma. Also reading or computer work, which require sharp sight, are not as frequently used as in the westernized world. Therefore, lower vision might not disturb the individual as early as elsewhere. In such settings, even a five item questionnaire, as suggested by Wang et al. can present a big challenge. (Wang et al. 1998)
Visual acuity testing is another simple tool which shall be discussed. VA alone is not considered a glaucoma screening test. But, according to Bowman, it could be the most practical test for the African setting, where advanced stages of glaucoma occur and are thus likely to affect VA. He suggests that all patients with visual acuities below 6/18 could be referred for thorough examination, if spectacles can be provided for refractive errors, and high-quality cataract surgery for immature cataracts. Thereby, some glaucoma patients may be picked up earlier than is presently the case. (Bowman & Kirupananthan 2006) Two preconditions (spectacles and cataract surgery) are assumed here which are not readily accessible in all settings. Nevertheless, visual E charts (as used in the present studies) or charts with symbols for illiterate patients are a rather simple, portable, and inexpensive tool for first orientation.

In the studies of this thesis an ICT cut-off of 21 mmHg was used as a definition of elevated IOP (normal range 11-21 mmHg). This cut-off is seen in most literature. Nevertheless, it is worth discussing which, if any, cut-off value should be used to screen most effectively for glaucoma. The following section briefly discusses possible IOP cut-off points. The AAO calls the value of 21 mmHg an “arbitrarily defined level”, because different studies give very inconsistent proportions of people with increased levels (range 13-71%). This “highlights the poor value of utilizing a specific IOP cut-off as a measure for screening and diagnosing POAG.” (AAO 2010b)

The results of the Bland-Altman analyses in section 3.6 and comparable literature showed that there was on average a 1 mmHg overestimation of GAT by ICT. This finding was taken as a basis for discussing a suitable cut-off point in this thesis, as explained in the following lines. Taken this 1 mmHg overestimation by ICT as given hypothesis, the study data was re-evaluated. It was looked at how many people were falsely indicated as elevated IOP above 21 mmHg, by changing the cut-off to 22 mmHg in ICT values. This implies that values of 21 mmHg in ICT actually present 20 mmHg in GAT. Therefore 22 mmHg would represent true 21 mmHg values, given a 1 mmHg overestimation of ICT against GAT.

In study A with a cut-off of 22 mmHg in ICT, 10% (n=20) instead of 11.5% (n=23) would have had increased IOP levels. Still all four individuals newly detected with
glaucoma (except NTG) would have equally been detected, as their ICT levels were above 21 and also above 22 mmHg. In study C, eleven out of all 106 people with levels over 21 mmHg in one eye would have been missed with 22 mmHg ICT cut-off. All except one patient (96.3%, n=26) of all 27 who were newly diagnosed with glaucoma would have been detected. This one missed case, despite his values of ICT 21/22 mmHg being on the lower edge of increased pressure, presented with rather advanced deep cupping and CDR of 0.8 and 0.7. In the broad IOP assessment study with 1,112 individuals, 12.8% instead of 13.8% would have been declared with raised IOP.

This result indicates that a cut-off rise of 1 mmHg for ICT would result in approximately 1% lower prevalence of raised IOP levels in this population, whereas about 1 in 30 (3.3%) glaucoma cases would have been missed. Most glaucoma cases, though, presented with IOP levels clearly exceeding 21 and 22 mmHg and would thus be detected with either cut-off point. Raising ICT cut-off to 22 mmHg at this setting therefore seems inefficient. Only a few at the lower margin to NTG would have been missed. Considering that CCT values in the respective population were found to be exceedingly low, this may result in underestimation of IOP values with wrongly low IOP values. Consequently, 21 mmHg as cut-off for ICT measurements at this setting seems appropriate.

Another approach to IOP cut-offs was mentioned in chapter 1.2.4, for which the 99.5th percentile of the normal population, e.g. for Malawi, could be evaluated. It enables practitioners to have a clearer orientation. From the dataset of study A by excluding all patients with glaucomatous findings, the 99.5th percentile of the mean ICT measurements of IOP would be 27 mmHg. Taking this cut-off in study A, for example, two out of five would have been missed, instead of one of five, which was a NTG. It could be reasoned to refer only those patients with IOP levels clearly exceeding 21 mmHg, e.g. over 27 mmHg in the case of this study. Ntim-Amponsah et al. came to the conclusion that in their Ghanaian sample, people with IOPs above 31 mmHg had a threefold higher risk to rapidly progress on to optic nerve damage compared to those with values below 32 mmHg. (Ntim-Amponsah et al. 2005) Such high cut-off (31 mmHg) certainly decreases the number of false positive referrals and increases the number of those in need of urgent treatment. At the same time it reduces the chance to detect cases in which treatment is not yet too late. It could be considered more an emergency detection instead
of screening for preventable, late-stage disease. It might be interesting to conduct a study with higher cut-offs.

After this discourse on possible screening tests in developing countries, age, intervals and target groups are specified in the following chapter.

4.5.2 Screening age and interval

Presumed as done in the introduction, that screening for the blinding disease glaucoma is useful and needed, it is crucial to discuss the age and intervals of the screening process. Researchers call for more studies regarding the best age at which to start screening, especially in individuals with a positive family history of glaucoma. (Ntim-Amponsah et al. 2004)

The German guidelines by BVA and DOG recommend screening with abovementioned examinations starting at the age of 40. Intervals should be every three years until the age of 64, and every one to two years after 65 years of age. If other risk factors apart from increasing age are present, intervals should be shortened. In case of glaucoma suspects or OHT patients under treatment, they recommend tonometry check-ups every third month. (BVA & DOG 2006) Another example of possible screening age in a high risk population is from the US. In 2002, the US Centers for Medicare and Medicaid Services initiated coverage for glaucoma examinations for African Americans 50 or older by eye care professionals. (AAO 2010b)

Especially in Africa the combination of two facts leads to specific conclusions regarding screening programmes. Firstly, glaucoma is more aggressive, it may occur faster and at an earlier age in Africans, as already mentioned in chapter 1.2.6. Secondly, glaucoma in general is a disease progressing with age. (Ntim-Amponsah et al. 2004) This leads to the conclusion that young AND old people should be considered in screening programmes among African populations. One possibility in the African setting is case-detection in hospitals and eye-camps in which every patient from 35 years onwards would receive an IOP measurement. (Hohmann 2011) Rotchford recommends for SSA to concentrate on advanced glaucoma stages, and thus do tonometry and disc assessment of every adult over the age of 40 who presents to an ophthalmologist. He
adds that in certain African populations, the age limit might have to be even lower, which is in accordance with abovementioned conclusion, but difficult to implement in the setting of low-income countries. (Rotchford 2005)

In the South-African study evaluating the prevalence of increased IOP and the usefulness of tonometry screening in a general practice, authors come to the conclusion that routine tonometry should be performed by every general practitioner. Their minimum request is once on every patient above 45 years. Ideally, tonometry should be repeated after 10 years. In cases of family history of glaucoma, tonometry checks should be done annually. Shorter screening intervals are recommended in diabetic or vascular pathology affected patients, who have an inert high risk of developing increased IOP and/or glaucoma. (van Niekerk et al. 2006) This idea stems from a comparably richer African country, but cannot be regarded as implementable in poorer countries due to lack of resources.

The findings of the present thesis could support screening at a younger age. Firstly, 18.2% of all POAG patients were between 25 and 39 years, and 9.1% between 18 and 24 years, resulting in 27.3% below 40 years. Among those were very young patients with rather advanced stages, as described in chapter 4.3.3, e.g. 20, 21, and 27 year olds who partly presented with unilateral blindness and large excavations. Nevertheless, the great majority (45.5%) was 60 years or older. If screening started at the age of 40, younger patients would have clearly been missed. Even screening after 25 years of age would have missed very young cases. One interpretation of these findings is that in the Malawian setting, and most likely in health centers in other developing countries, screening for glaucoma should ideally start early, at the age of 20 or 25 years at latest. Realistically though, it might not be realizable due to lack of resources.

A suggestion which corresponds well to the present findings of this thesis is made by Essuman and Ntim-Amponsah. In their hospital-based study from Ghana they determined the age, timing, and associated factors for glaucoma evaluation as part of medical eye examination in an ophthalmology clinic. They criticise that glaucoma screenings often focus on those over 40 years of age, even though it is known that in Africans the disease occurs earlier. Further they find fault with the lack of evidence as
to when to start screening in African populations. They found an upsurge of glaucoma prevalence after the age of 24, which led them to the conclusion that **25 years** can be an appropriate age to start glaucoma assessment. Their recommendations are visualized in Table 15. (Essuman & Ntim-Amponsah 2012)

<table>
<thead>
<tr>
<th>Age and risk factor</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-30</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>20 and above with eye complaints</td>
<td></td>
</tr>
<tr>
<td>31 and above</td>
<td>Yearly</td>
</tr>
<tr>
<td>Any age with positive family history</td>
<td></td>
</tr>
</tbody>
</table>

Screening is recommended **every two years in people above 25 years**. In case of eye complaints, screening should start at 20 years. **At the age of 31** and above, screening intervals should be shortened and therefore **yearly** screening intervals are suggested, and at any age in people with positive family history for glaucoma. In conclusion their glaucoma screening guidelines, with routine measurement of IOP and evaluation of the optic disc biomicroscopically in the setting of eye hospitals, seems close to ideal but highly out of reach in most settings of the developing world.

In theory, the suggestions could be regarded as transferable to the context of LSFEH, Malawi. In reality, less ambitious goals will be more practicable in the actual setting, which is dealing with shortness of money, staff and equipment. Screening intervals and repeated visits of one and the same individual are highly impracticable and unlikely to be successful in financially restricted contexts. Therefore, a modified proposal is summarized in chapter 4.6.

### 4.5.3 Target groups

Lawan speaks of a “need” to find definitions on whom to screen, as there is no justification to screen the population on a large scale. (Lawan 2013) Rather, target groups should be determined to render screening more (cost-) effective. (AAO 2010b)
AAO lists “African Americans and Hispanics” as possible target groups. (AAO 2010b) Consequently, Africans as such can be considered a target group. As this is not (yet) practicable on everybody in an all-African environment, further target groups need to be established for Africa. Focusing on late stage disease has already been discussed in chapter 4.5.1 as one possibility to channel the process. Further suggestions for target groups are:

- Family history of glaucoma (Wolfs et al. 1998) (AAO 2010b) (Flammer 2001)
- First degree relatives (Lawan 2013)
- Older adults (AAO 2010b)

One target group are people with a positive glaucoma family history. As previously mentioned, retrieving information about patient’s family history of certain diseases is not an easy task to do, neither in the western nor in any other part of the world. Nevertheless, cultural differences have to be taken into consideration when trying to access this data. Patients may not know their own or family’s history of disease, they may not be educated about diseases or the modern concept of medicine. It might not be appropriate in a certain society to admit and talk about one’s own or family members’ diseases. It further might not be part of family discourse at all, due to stigmatisation or other disadvantages to the affected individual. Or traditional beliefs and explanations for an individual’s illness might be a patient’s underlying belief, which might not willingly be shared with a modern clinician. This “general culture of keeping diseases as personal” also between family members and abovementioned reasons, are all possible explanations why low numbers of positive family histories could sometimes be recorded. (Essuman & Ntim-Amponsah 2012) This makes positive family history a challenging aspect.

A second difficulty after finding out about patients’ family history is to successfully invite family members for (regular) check-ups. Even when contacted through the affected person and offered free examination, relatives in a rural setting in Tanzania were unlikely to report for examination. Those living further away did not present for exam at all, and only 10% of those from the same district came for examination, showing that costs for transport can be a main burden. The allocation of costs to the high-risk group
of family members of glaucoma patients does not seem feasible and free transport and examination has to be guaranteed, at best by the state through the clinic. Otherwise, the appeal to come for a medical check-up in a poor society is most likely going to fade away without consequences. (Munachonga et al. 2007) (Friedman 2007)

Wolfs et al. advice that glaucoma screenings among relatives of glaucoma patients should first and foremost assess CDR, as this was the earliest and most prominent parameter to detect glaucoma. The lifetime risk to develop glaucoma was 22% in relatives. This was ten times higher than in the control group. Their data suggested that one sixth of all glaucoma could be due to genetic inheritance. (Wolfs et al. 1998)

Regarding the target groups suggestion of family history and first degree relatives of glaucoma patients, no suggestion can be deduced from the data of this thesis, because no applicable results were collected. Even though the question of family history of eye disease or vision loss was posed, most people were unable or unwilling to give clear information. Research on this topic is currently done at LSFEH and will be worthwhile.

A supplement on the topic on inheritance is the current trend towards genetic screening. Studies from Africa, which analysed e.g. mutations in myocilin, optineurin, or mitochondrial DNA, have so far not been convincing. In economically weak areas, it is further not a realistic and practicable concept. (Lawan 2013)

As far as the target group of older aged people is concerned, recommendations have already been proposed in chapter 4.5.2. One aspect which is connected to age and glaucoma is cataract. In our study 45.5% of POAG patients had bilateral cataract. To avoid the risk of missing glaucoma patients due to cataracts every patient diagnosed with a cataract should also get an IOP check and a fundus assessment. Therefore, a modified version of Table 15 on glaucoma screening recommendations for the context of LSFEH is illustrated in Table 16, considering this aspect. One major aspect, though, is the fact that a general screening of the population is unrealistic, but a screening of those already presenting to the eye clinic due to ocular problems could as well be checked for these two diseases.

A joint screening for both diseases has also been promoted by Cook. He suggests screening for cataract and glaucoma together in primary care clinics by visual acuity
testing and at secondary level by using a test combination of optic disc and pupil assessment. (Cook 2009) Therefore, one suggestion is to include glaucoma screening in general screenings for eye diseases among the elderly. (AAO 2010a) Already Wang et al. in 1998 criticised to concentrate on a single disease during screening instead of several at once. Screening for several age-related diseases at once, including glaucoma, can be of benefit to the individual and to the clinician as it is efficient and time-saving. The inevitable precondition would be a test able to detect several diseases at once. (Wang et al. 1998) To this date, though, there is no single test, which could meet this demand. Only clinicians themselves can achieve this with their visual diagnostic skills.

One additional factor in screening programmes is gender. In the setting of the present thesis, gender imbalance was observed and explained by cultural as well as socio-economic barriers for women in Malawi. According to Kayange et al., this imbalance should be tackled by health intervention programmes, also for glaucoma. (Kayange et al. 2014)

The data collection at the OPD of LSFEH for this thesis showed contrasting figures. 58% females against 42% males attended the OPD. Women at the OPD were mostly below age 60 (84%), of which 58% were between 18 and 39, and only a minority was older than 60. Contrarily, 55% of POAG patients were male. Thus, despite a female majority at the OPD, POAG was more common among male attendants. Therefore, the recommendation given in chapter 4.6 is to address both genders equally during glaucoma screening.

4.5.4 Training (non-)ophthalmologists

Mermoud, president and founder of the charity “Vision For All” calls for more training of eye doctors. (Kingman 2004) Education and awareness is required among ophthalmologists as well as clinical officers (specialist nurses) and non-ophthalmologists at all levels. At primary and secondary health care centres, personnel, especially in Africa, could be trained to detect and refer patients suspicious for glaucoma. As late stages are easier to diagnose, non-ophthalmologists can be equipped with skills needed to diagnose these stages. Tonometry and optic-disc assessment can be taught and if used routinely, with clear and easy criteria for referral, higher detection rates of glaucoma can be
achieved. (Kayange et al. 2014) (Rotchford 2005) For comparison, in the UK 99% of referrals to eye hospitals of glaucoma suspects are initiated by optometrists at primary health level. (Spry & Sparrow 2005)

Cook gives precise suggestions for glaucoma detection in rural Africa. At primary level, employees (clinic nurses, community health workers, traditional healers, etc.) should screen everyone 40 years or older at least once every two years. In case of reduced VA in one or both eyes, plus black pupil (in the sense of non-present cataracts), patients shall be referred to secondary level. At secondary level, ophthalmic nurses and ophthalmic medical assistants should perform tonometry and funduscopy with CDR assessment on everyone 40 years and older at least once every two years. All glaucoma suspects or cases should be seen at tertiary level by ophthalmologists for diagnostic confirmation and treatment. (Cook 2001) These ambitious propositions must nevertheless be seen in the light of limited resources in rural Africa and the fact that many other including life-threatening diseases are often not covered by health programmes.

Furthermore, if ophthalmologists and any other health worker were sensible to the possible joint appearance of the age-related diseases glaucoma and cataract, it could lead to higher detection rates of glaucoma. Patients are urged to seek medical help as cataract is the “pain”, to recite Lawan’s words, in the sense of blurred or reduced vision or photosensitivity. (Lawan 2013) If trained staff jointly looks for cataract and glaucoma, every visit to a health centre may lead to the detection of asymptomatic glaucoma.

Raising the awareness among eye care providers for glaucoma and its detection during comprehensive eye exams, especially in high-risk populations, is thus an important step towards more effective case detection. In the same manner, education of the general population about glaucoma and the meaning of regular check-ups may contribute to earlier detection. (Maul & Jampel 2010)

Another aspect, which respects doing research in a different culture, is the role of traditional healers. On local levels, they treat many common (eye) diseases and are likely to be frequented first by affected individuals. Especially in rural areas, they are regularly consulted. It is also for practical reasons, because there are traditional healers in almost every village (one healer per 350 people), but only a few health care workers (one
health staff member per 2030 people). (Courtright et al. 1994) Even though these figures are out-dated, the principles are valid in todays, especially rural Malawi.

In Kayange et al.’s study, 25% of patients admitted the use of traditional medicine before attending the eye clinic. This number is estimated to be higher in reality, as traditional medicine is possibly denied in the hospital setting. It may be benefitting to all parties involved, if there was more communication and collaboration between traditional healers and clinicians. (Kayange et al. 2014) Examples from other health projects showed that training and working together with healers generated positive changes in attitudes and behaviour among traditional healers and health care employees. An option would be to train healers in recognizing emergency cases which should be referred to the hospital, and motivate them to use safe, non-harmful traditional practices. For instance support face washes and steam baths, but not the application of plants directly into the eye, which are the three common traditional treatments for eye complaints. (Courtright et al. 1994) Experiencing interest from (non-) governmental health agencies and by positive feedbacks from referred patients, healers are reported to feel more appreciated. (Courtright 1995)

Suggestions for more effective screening and glaucoma detection were made at all levels, from traditional medicine to primary ophthalmic centres, taking into account the results of this study as well as opinions and recommendations from other authors. Target groups, appropriate ages, and screening intervals have been elaborated on. It is apparent that international and state money, the effort of health workers and specialists and further research are needed for more successful glaucoma detection, and the prevention of blindness.

4.6 Conclusions for glaucoma screening and detection at LSFEH

After looking at screening recommendations for developing countries in literature, it became evident that glaucoma as such is a disease which is hard but important to screen for. Yet, no convincing concepts exist. Taking the right combination of screening tests and target groups is important, even more so in the context of Africa. Therefore, chances and challenges in the clinical practice of the Malawian tertiary eye center LSFEH are
specified, recapitulating conclusions of the prior discussion. It has to be stressed, that the following recommendations only apply to the setting of a tertiary health institution and are not intended for primary or other basic health settings. Eventually, recommendations for better glaucoma detection at LSFEH is established and illustrated in Table 16 below.

4.6.1 Guideline proposal for glaucoma screening at LSFEH

As mentioned in chapter 4.5.1 no recommendation for a general population-based ICT screening in Malawi or for all patients at LSFEH can be concluded. Yet, LSFEH is a tertiary eye hospital with a highly motivated staff and glaucoma detection is an important aim. Therefore, recommendations shall be made for better and more effective glaucoma screening in the form of a guideline proposal for the practice at LSFEH according to the data of this thesis. They are conclusively summarized in Table 16.

<table>
<thead>
<tr>
<th>Age and risk factor</th>
<th>Examination</th>
<th>Interval*</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 and above</td>
<td>ICT + Funduscropy</td>
<td>Every three years**</td>
</tr>
<tr>
<td>- if presenting with impaired vision at the OPD</td>
<td>Focused Cataract &amp; Glaucoma check-up</td>
<td></td>
</tr>
<tr>
<td>- if cataract present</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* at least one measurement at first visit, interval is recommended if possible
** if IOP > 21mmHg or suspicious fundus

Accordingly, at the OPD of LSFEH, every patient with 40 years and above, presenting at the OPD with impaired vision should receive ICT measurements and funduscropy. To avoid the risk of missing glaucoma patients due to a fast cataract diagnosis, every patient with cataract should also get an IOP-check and a fundus assessment.

Combining ICT and funduscopy can possibly rule out missing NTG, which was one of the shortcomings of the present study and avoiding the low sensitivity and specificity of ICT alone. During examinations, signs of glaucoma and cataract should be jointly looked for.
21 mmHg as cut-off point is considered an appropriate ICT value for practice, so patients above 21 mmHg in three consecutive measures should be considered suspicious. It has to be noted though, that very high IOP values could be inaccurate, and should be double-checked with GAT.

In case of suspicious IOP or fundus findings, they should be checked regularly with ICT and funduscopy in intervals of two or three years, as indicated above. It is obvious that at this setting, the suggestion of intervals is not totally realistic and might not be followed by many individuals. Therefore it needs to be stressed again, that abovementioned target groups should at least get one ICT measurement and funduscopy done at their first visit to the OPD.

It was mentioned in chapter 4.5.2, that especially in Africa, due to the combination of the fact that glaucoma is an age-related disease and the special dynamic of glaucoma development in African populations, detection should focus on old people. After 40 years of age, Malawians appear to have an increased risk of glaucoma development, as the thinnest CCTs, one potential glaucoma risk factor, were recorded in this age group. Further, because in most glaucoma patients, IOP starts rising between 40 and 50 years, treatment needs to be initiated at this stage to prevent further damage. (Flammer 2001) (Kingman 2004) Also, the detection rate was 4% in the group above 40 years, in comparison to 2.5% in the total sample. For all these reasons and realistic purposes, even though it would be ideal to also check young patients at the OPD of LSFEH, the cut-off point was set at 40 years.

Special alertness is further recommended when being confronted with elderly patients, since every opportunity to examine them should be seized to screen for cataract AND glaucoma, especially if patients present with visual complaints. This combination should become an automated routine at LSFEH during eye examinations of patients above the age of 40.

Thin CCT in line with high IOP were found as risk factors for the development of glaucomatous damage to the optic nerve, with a high risk of blindness in the study population at LSFEH. CCT at LSFEH has been found in the conducted study to be extremely thin. Yet, it cannot be recommended to do CCT assessment on every patient,
as it is very time-consuming and unfeasible. Rather, ophthalmic staff has to be aware of this low CCT average, especially among glaucoma patients, because IOP values might be underestimated, and thin CCT puts those patients at special risk of developing optical nerve damage. It was recommended to measure CCT before setting individual target pressures for therapy, as it might have to be targeted lower in case of very thin CCT findings. (Boehm 2011) (Hoffmann et al. 2013) Thus, general awareness about thin CCTs should to be spread among all ophthalmic staff members at LSFEH to correctly interpret their examination results. It would be ideal and advisable to take CCT measurements once before or during treatment of glaucoma patients for appropriate target pressure definition. Its practicability needs to be proven.

In general, increased IOP levels and POAG was slightly more common among males, and therefore men above 40 should be looked at carefully. Women were presenting less often to the OPD above the age of 60 and more often between the age of 25 to 59 (66.4%). If women rarely attend the clinic at older ages, they should be examined closely at any time they appear. This fact can be used effectively at the OPD, as this bears the chance to find women with earlier glaucoma stages, if examined carefully by well-trained and sensitised staff. Combining these findings, careful attention should be given equally to both sexes between 40 and 60 years of age, as there is a realistic chance to not only find late, but also early-to-medium stages.

After looking at possible target groups and examination methods for reasonable glaucoma detection at LSFEH, some special challenges at this particular setting shall be highlighted.

4.6.2 Special considerations regarding glaucoma management at LSFEH

Great challenges in glaucoma assessment at LSFEH are the presence of only one worn-out ICT and only a few GATs. Perimetry was not available at LSFEH during the time of the study and alternatives should be considered and implemented in the meantime. Instead of optic nerve photographs, which cannot be taken of every glaucoma patient upon every visit, a schematic drawing as recommended by the AAO is a practicable measure for better documentation of fundus findings. (AAO 2010b)
In order to achieve a higher glaucoma detection rate, it would be ideal to train more clinical officers and other appropriate staff members in funduscopy, GAT and ICT. ICT is a quick and well-tolerated tool, which can be taught to receptionists and other non-ophthalmological staff members. CDR assessment as well as GAT should be taught early in ophthalmology education and should be mastered already by junior professionals.

Further, public health education about glaucoma should be promoted, e.g. by national campaigns, posters or through health education at schools, communities, and among other health care workers, as suggested similarly by Schulze Schwering et al. Major burdens were costs for public transport. If transport and examinations cannot be offered free of charge, patients or family members of glaucoma patients are unlikely to present regularly, if at all, for check-ups. Thus, national efforts should be strengthened to support these measures for prevention of blindness. (Schulze Schwering et al. 2014)

Besides strengthening the awareness among health workers, compliance of patients can be ameliorated by stressing the seriousness of the disease. It has to be explained that even in absence of symptoms or pain, the presence of the disease may be detrimental. Painlessness is a feature which makes it difficult to convey the seriousness of glaucoma and convince affected people to spend money on treatment. (Kosoko et al. 1998)

Another challenge in the general management of glaucoma is poor compliance to treatment, apart from a general poor availability of treatment options and provisions. (Kyari et al. 2013) In case of apparent inability or unwillingness of patients to comply to or pay regular therapy with medication, surgical options should be considered earlier than might be the case in settings where medication is readily available. An article on glaucoma management in Africa states that surgery “is almost always the correct treatment in Africa, where medical therapy throughout the patient’s lifespan is impractical”. (Bowman & Kirupananthan 2006) Besides the practical fact, surgical solutions can be cheaper for individuals, national and global economies, compared to long term glaucoma treatment. Especially in economically challenged countries, prevention of high treatment costs should be a major concern, since not even developed economies can afford the costs of preventable blindness. (Adio & Onua 2012)
A big challenge for treatment of glaucoma at LSFEH is the reported fact that medications are often less effective in individuals of African descent than in other populations. (Tielsch 1991) Also surgical outcomes are less successful in Africans as well as in Asians, due to a stronger and more rapid scarring process of tissues. (Kingman 2004) Also in this respect, further research about treatment options in these populations is desirable.

As previously mentioned in chapter 4.2, 10% prevalence of increased IOP among apparently healthy populations in this African region may be appropriate. A slightly higher prevalence of 11-18% among ophthalmologic patients seems to be a realistic approximation, which may be used as a basis for further discussions or consecutive researches.

As a US professor of ophthalmology expresses, it is very positive that in general, blindness caused by POAG has been reduced. Yet, still too many do suffer this fate, especially in less developed countries. Therefore, further research on glaucoma is strongly supported. (AAO 2014) For Malawi it is desirable that the proposed recommendations may stimulate further discussion and verification in theory and practice on-site.

### 4.7 Limitations of study design and data collection

In every clinical study, limitations and controversies are inevitable. Firstly, an absolute diagnosis of glaucoma cannot be given due to limitations of examination possibilities. The lack of visual field testing devices and regular documentation, e.g. of fundus findings for the estimation of disease progression, are reasons for partly rather subjective diagnoses. Even though glaucoma diagnosis by CDR assessment is in itself subjective and is different from clinician to clinician, the limited technical possibilities for diagnosis and documentation are an added complication. Foster et al. mention the absence of perimetry and a diagnosis of glaucoma which is only based on CDR and tonometry, may lead to an underestimation of glaucoma cases. (Foster et al. 2002) Nonetheless, the presence of the ASOCT due to donation was an important feature to detect possible causes of glaucoma. The true prevalence of glaucoma at LSFEH might thus be higher than detected throughout the studies. In general terms, it is possible that some cases
were missed and others might be diagnosed incorrectly. Nonetheless, the thesis gives an approximation to the disease patterns and numbers in this region of Malawi.

Secondly, a major constraint in producing significant and comparable data is the fact that various definitions exist for several of the used parameters. Blindness and glaucoma itself are defined differently in existing literature. In developing countries, due to limited possibilities, definitions and diagnoses cannot be made in the same way and perfection as elsewhere. Different methods are used to record e.g. VA, IOP, or CDR. Furthermore, study samples are often small, and especially among the scarce data from Africa, samples often represent a rather confined portion of a population. This leads to discussions and comparisons of numbers and figures which are often not based on the same standards and definitions. (Kyari et al. 2013)

A third limiting factor was the momentary pressure documentation, as ICT and GAT measurements were recorded only at one point in time. Some patients were invited to come back for check-ups, of which some did and some did not return. It was not recorded in the data of this thesis, as it was not possible to organize and survey it in the limited period of time. Furthermore, the detection of NTG was only possible in the study A, as people with normal IOP levels were excluded in study C. NTG or those glaucoma patients who presented with normal IOP values at that specific time, but have e.g. nocturnal pressure spikes, will have been missed. This represents a further indication for actually higher numbers of glaucoma at LSFEH then detected in this thesis.

In the discourse on IOP assessment and diagnosis of glaucoma, it has to be added that in those cases in which patients presented with very high pressures, their cornea was often too hazy to access the fundus. Still they were defined as glaucoma cases, since their pressure and thus the likelihood of glaucoma put them at high risk. Often patients with hazy corneas, and also those without hazy corneas but high pressures, were sent for check-up. As mentioned before, this data, though, has not been recorded.

Nevertheless, there were cases in which raised IOP levels were detected at first visit, and normal values upon the second visit. Still, it was recorded as “raised IOP” due to the findings at first presentation. It was not possible to keep track of all patients who
returned for check-ups, because second assessments were not always done by the personnel of the study, but also by other staff at LSFEH.

All data regarding age has to be looked at in light of the fact that the exact date of birth is often not known and not correctly documented. Especially in the older generation, only rough estimates about age can be given. A common answer on their age among patients was “about 50 years”. For statistical evaluation we had to record this approximated age with a specific number, which might not represent the true age. In case of the female patient with 112 years, it can therefore not be claimed with certainty if this information was correct.

Partial inaccuracies have to be assumed in terms of GAT measurements as well as VA assessment. Further, some of the patients were examined for the first time in their life, especially as GAT is a procedure which requires training and accustoming on the part of patients. Practical application was sometimes difficult, and therefore measurement inaccuracies are possible in this respect. As far as VA testing is concerned, it was sometimes difficult to instruct patients correctly, and often they did not fully understand the tasks. Thereby, some data on VA might be imprecise.

On the one hand, the sample selection of the studies cannot be considered to be randomized, and does not raise the claim to represent the general Malawian population like a population-based epidemiological survey would. On the other hand, this sample produced a much higher yield of the targeted glaucoma cases than would have been obtained from a broad population screening. The sample is thus partially biased. Firstly, because it was hospital-based and even the sample of healthy people was selected on the premises of the hospital for practical reasons. Secondly, the sample represents a poorer fraction of the population as the hospital is public and frequented more by those who cannot afford to pay for private clinics. Blantyre is an urban centre and thus patients presenting to LSFEH do not necessarily represent rural populations.

Many important additional factors for the development of glaucoma have not been included in this study. Myopia, vascular pathologies, high blood pressure, diabetes, or the use of steroids could have a great influence and more research has to be done to evaluate these patients as potential target groups in glaucoma screenings. A possible
obstacle to this effort might be that patients often do not know their blood pressure, diabetic, or sickle cell status. (Ntim-Amponsah et al. 2005)

Some glaucoma cases presented with a good CDR of e.g. 0.2 in at least one eye. This can be explained firstly by the fact that diagnosis of glaucoma was also given due to very high IOP findings only, yet without suspicious CDR. This was justified because such high IOP puts those patients at high risk for the future development of glaucomatous changes. Further, in case of secondary glaucoma or POAG which affected only one eye, the other, unaffected eye of this patient is also recorded.

A remark was made by Nangia et al. that large optic discs, commonly found in black patients, might lead to an over-diagnosis of glaucoma. (Nangia et al. 2013) The fact that all clinicians performing optic disc assessment in the present study are experienced and accustomed to the African population, this misjudgement can be regarded unlikely.

A further comment is dealing with the treatment, which was prescribed to patients newly diagnosed with glaucoma. Even though consequences and seriousness of the disease were thoroughly explained in local language, it has to be assumed that not everybody will have bought the needed drugs. The hospital pharmacy was supposed to provide glaucoma medications, but they were regularly out of stock. Thus, patients were urged to buy it on their own expenses. In many cases, this is unlikely to have happened due to lack of financial resources and compliance, particularly since treatment is usually necessary for the rest of their lives. The same doubt exists in respect to regular follow-up visits.

In terms of statistical analysis it is a limiting factor to the expression of significance that for example in the dichotomous variable of glaucoma diagnosis the two groups are comprised of very different sample sizes of 1081 healthy against 27 glaucoma cases.

Lastly, it cannot be anticipated whether the proposed guidelines are workable for glaucoma detection at LSFEH. They may nevertheless stimulate further discussions, as well as verification in theory and practice among ophthalmologists and health care workers at LSFEH, elsewhere in Malawi and other countries in the developing world.
5 Summary

Glaucoma is the second leading cause of blindness worldwide, in Africa and also in the African country Malawi. It is said to cause 8 to 12% of global blindness. The prevalence of glaucoma in Africa is estimated to be about 4.79%. According to the research, there is no scientific data for Malawi. This thesis was designed to create a database for this African country with information regarding features of healthy and glaucomatous eyes, with a focus on intraocular pressure (IOP), optic disc appearance and central corneal thickness (CCT). It further analysed the prevalence of increased IOP above 21 mmHg, as this is one of the major risk factors for the development of glaucoma. The prevalence of glaucoma in Malawi were approximated.

The clinical research consisted of three cross-sectional studies, carried out between August and October 2014 at Lions Sight First Eye Hospital (LSFEH) in Blantyre, Malawi. The first study (A) comprised 200 people randomly recruited on the hospital premises, who were presently not seeking medical help for visual disturbances and without a known diagnosis of glaucoma or high IOP. The intention was to gather data of the average Malawian population as a basis for further studies. Results indicated the prevalence of increased IOP and the number of glaucoma cases among them. The second study (B) consisted of 1,112 patients at the outpatient department (OPD) of LSFEH. It aimed at getting a maximum number of IOP measurements by ICare tonometry (ICT), detecting the average IOP and prevalence of increased IOP. The third study (C) consisted of 106 patients with increased IOP values in three consecutive ICT measurements in study B. This enabled to detect the actual prevalence of glaucoma among those suspicious by ICT values. The data of glaucoma patients was analysed separately to describe characteristics of glaucomatous eyes.

The thesis resulted in conclusions regarding the effectiveness of an ICT screening for glaucoma and possible guidelines for glaucoma screening at LSFEH. Results were evaluated in mean, median, minimum-maximum-ranges, frequencies, and percentages. Subgroups were formed using SPSS, e.g. by glaucoma diagnosis, gender, age above and below 40 years or patients with CDR above 0.8 in funduscopy. Correlations were calculated for all metric variables.
The prevalence of increased IOP above 21 mmHg among the non-glaucomatous sample (A) was 10%. Among ophthalmologic patients at the OPD (B) the prevalence was 11 to 18%, depending on gender and age. The general glaucoma prevalence in the healthy sample was 2.5%, whereas in the age group above 40 years it rose to 4.6%, which is in accordance with prevalence numbers for Africa. Glaucoma prevalence among those with increased IOP (C) was 25.5%.

The main glaucoma type of all examined patients from study A and C was primary open-angle glaucoma (POAG) with 60 to over 70%. CCT values were found to be thinner than in other data from African populations. Mean CCT of the healthy sample was 509.2 µm and among POAG patients it was 516.2 µm. In study C the group with a CDR 0.8 or worse had a CCT mean of 501.6 µm. The thinnest corneas were found among POAG patients above the age of 40 with a mean of 494.5 µm.

In study A the ICT sensitivity was 80% with a specificity of 90%, a positive predictive value of 17% and negative predictive value of 99.4%. Therefore, ICT alone cannot be regarded as a useful screening method. No recommendation for a general ICT screening of the Malawian population or all patients at the OPD of LSFEH can be made.

A guideline for a focused glaucoma screening at the OPD of LSFEH was developed, using a combination of screening methods. Accordingly, every patient of 40 years and above, presenting at the OPD with visual impairment should receive ICT measurements in combination with funduscopy. To avoid the risk of missing glaucoma due to fast cataract diagnoses, every patient with cataract should get an IOP and a fundus assessment. In case of IOP above 21mmHg or suspicious fundus findings, patients should be checked regularly with ICT and funduscopy in intervals of two to three years. Due to financial obstacles, it will most likely be difficult for many patients to follow these intervals. Therefore it is recommended, that abovementioned target groups should at least get ICT measurements and funduscopy at their first visit.

This guideline shall encourage a focused glaucoma management at LSFEH and thus avoid cases of preventable blindness.
German Summary


Die klinische Forschung bestand aus drei Querschnittsstudien, welche zwischen August und Oktober 2014 an der Augenklinik „Lions Sight First Eye Hospital“ (LSFEH) in Blantyre, Malawi, durchgeführt wurden. Die erste Studie (A) umfasste 200 zufällig ausgewählte Personen auf dem Krankenhausgelände, die aktuell nicht wegen Sehbehinderungen einen Arzt aufsuchten bzw. kein bekanntes Glaukom oder erhöhten IOD hatten. Dadurch sollten Werte der durchschnittlichen Malawischen Bevölkerung erhoben werden, die als Basis für weitere Studien dienen können. Die Ergebnisse zeigten die Prävalenz erhöhten IODs und der Glaukome in einer gesunden Malawischen Studienpopulation. Die zweite Studie (B) bestand aus 1,112 Patienten, die sich in der Ambulanz der Augenklinik befanden. Sie zielte auf eine möglichst große Zahl von IOD-Messungen mittels ICare Tonometer (ICT) ab, um einen Durchschnitts-IOD und die Prävalenz erhöhten IODs zu detektieren. Die dritte Studie (C) umfasste 106 Patienten, die in drei aufeinanderfolgenden ICT-Messungen im Rahmen der Studie B einen erhöhten IOD hatten. Dies ermöglichte die Glaukomprävalenz unter denen zu bestimmen, die suspekte IOD-Messungen aufwiesen.

In der Arbeit wurde der Nutzen von Glaukom-Screenings mittels ICT ausgewertet und eine Screening-Leitlinie für Glaukom am LSFEH erstellt. Die Ergebnisse wurden mit Mittelwert, Median, Minimum, Maximum, Häufigkeiten und Prozenten angegeben. Mit

In Studie A wiesen 10% der untersuchten Personen einen erhöhten IOD auf. Unter den Patienten in Studie B waren es 11 bis 18%, abhängig von Alter und Geschlecht. Die Glaukomprävalenz betrug 2.5%. In der Gruppe der über 40-jährigen waren es den Prävalenzzahlen in Afrika entsprechend 4.6%. In Studie C betrug die Prävalenz 25.5%.

Das primäre Offenwinkelglaukom (POWG) stellte mit 60 bis 70% die Hauptform der Glaukome in Studie A und C dar. Die ZHD-Werte waren geringer als in anderen afrikanischen Populationen. Sie betrugen unter den Gesunden durchschnittlich 509.2 µm und unter POWG-Patienten 516.2 µm. Patienten mit einer CDR von 0.8 oder mehr wiesen eine durchschnittliche ZHD von 501.6 µm auf. Die dünnsten ZHD-Werte von 494.5 µm wurden unter den POWG-Patienten über 40 Jahren gefunden.

In Studie A wurde eine ICT-Sensitivität von 80% und eine Spezifität von 90% errechnet, mit einem positiv prädiktiven Wert von 17% und einem negativ prädiktiven Wert von 99.4%. ICT-Messungen allein können nicht als adäquate Screening-Methode gewertet werden. Ein generelles Screening aller in Malawi oder auch aller Patienten im LSFEH erscheint nicht sinnvoll. Vielmehr wird ein fokussiertes Screening mit einer Kombination von Methoden vorgeschlagen.

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7 Author’s contribution to the present study

Declaration of authorship for my dissertation entitled:

“Prevalence of increased intraocular pressure and presentation patterns of glaucoma at a tertiary hospital in Malawi, South-East-Africa”

I hereby certify that this thesis has been composed by me at the University Eye Hospital Tuebingen under my supervisor Prof. Dr. med. Martin Spitzer and is based on my own work, unless stated otherwise. No other person’s work has been used without due acknowledgement in this thesis. I have clearly marked and acknowledged all quotations or references that have been taken from the works of others. All secondary literature and other sources are marked and listed in the bibliography. The same applies to all charts, diagrams and illustrations as well as to all online resources. The study design and drafts were corrected by Prof. Dr. med. Martin Spitzer and Dr. med. Johanna Müller as academic tutor.

The clinical part of the study was executed by me with assistance by Dr. med. Johanna Müller and ophthalmologists from Lions Sight First Eye Hospital (LSFEH), Malawi, namely Dr. Petros Kayange, Dr. Moira Gandiwa und Dr. Patty Mapamboli. Translation from English to Chichewa was done by Herbert Thole and Boston Zimba, local medical students.

Statistical data analysis was done by me after consultation with Aline Naumann from the Institute of Clinical Epidemiology and Applied Biometry at Tuebingen University.

This thesis was not previously presented to another examination board and has not failed any doctoral examination procedure before.

__________________________  ______________________________
Place, Date                      Signature
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9 Appendix

9.1 List of Figures

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9.3.1 Summary of all study findings

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<table>
<thead>
<tr>
<th></th>
<th>Study A Healthy</th>
<th>Study B OPD</th>
<th>Study C IOP &gt;21mmHg</th>
<th>Study A&amp;C POAGs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number</td>
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<td>1,112</td>
<td>106</td>
<td>22</td>
</tr>
<tr>
<td>Gender distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>53.0</td>
<td>58.2</td>
<td>50.9</td>
<td>45.5</td>
</tr>
<tr>
<td>Male (%)</td>
<td>47.0</td>
<td>41.8</td>
<td>49.1</td>
<td>54.5</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean / Median</td>
<td>35.3 / 32</td>
<td>41.2 / 36</td>
<td>46.6 / 43</td>
<td>52.0 / 54</td>
</tr>
<tr>
<td>&lt;40 n (%)</td>
<td>135 (67.5%)</td>
<td>617 (55.5)</td>
<td>44 (41.5%)</td>
<td>6 (27.3%)</td>
</tr>
<tr>
<td>&gt;=40 n (%)</td>
<td>65 (32.5%)</td>
<td>495 (44.5)</td>
<td>62 (58.5%)</td>
<td>16 (72.7%)</td>
</tr>
<tr>
<td>Age group n (valid %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>40 (20.0)</td>
<td>193 (17.4)</td>
<td>14 (13.2)</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>25-39</td>
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<td>31 (29.2)</td>
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<td>-</td>
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<td>1 (0.9)</td>
<td>-</td>
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<td>IOP (ICT / GAT)</td>
<td>(only ICT)</td>
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<tr>
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<td>16.6 / 15.4</td>
<td>16.6</td>
<td>26.7 / 25.9</td>
<td>30.2 / 30.3</td>
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<tr>
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<td>15.5</td>
<td>24.5 / 24</td>
<td>27 / 26</td>
</tr>
<tr>
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<td>16.5 / 15.3</td>
<td>16.8</td>
<td>26.0 / 25.4</td>
<td>29.0 /29.3</td>
</tr>
<tr>
<td>R_Median</td>
<td>16 / 15</td>
<td>16</td>
<td>25 / 24</td>
<td>27 / 26</td>
</tr>
<tr>
<td>L_Mean</td>
<td>16.6 / 15.5</td>
<td>16.4</td>
<td>27.4 / 26.5</td>
<td>31.4 / 31.3</td>
</tr>
<tr>
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<td>16 / 15</td>
<td>15</td>
<td>24 / 24</td>
<td>27 / 26</td>
</tr>
<tr>
<td>IOP &gt;21mmHg no. (%)</td>
<td>23 (11.5)</td>
<td>154 (13.8)</td>
<td>all</td>
<td>all</td>
</tr>
<tr>
<td>Dx</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total n (%)</td>
<td>5 (2.5)</td>
<td>27 (2.4)</td>
<td>27 (25.5)</td>
<td>all</td>
</tr>
<tr>
<td>POAG</td>
<td>3 (1.5)</td>
<td>19 (17.9)</td>
<td>all</td>
<td></td>
</tr>
<tr>
<td>PEX</td>
<td>1 (0.5)</td>
<td>3 (2.8)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Secondary glau</td>
<td>0</td>
<td>5 (4.7)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>NTG</td>
<td>1 (0.5)</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Suspects</td>
<td>5 (2.5)</td>
<td>20 (1.8)</td>
<td>19 (17.9)</td>
<td>-</td>
</tr>
<tr>
<td>CCT (µm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Mean / Median</td>
<td>509.2 / 507.5</td>
<td>527.8 / 527</td>
<td>504.7 / 505</td>
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</tr>
<tr>
<td>R_Mean / Median</td>
<td>508.9 / 506.5</td>
<td>523.8 / 523</td>
<td>514.4 / 504</td>
<td></td>
</tr>
<tr>
<td>L_Mean / Median</td>
<td>509.5 / 508.5</td>
<td>531.7 / 531</td>
<td>518 / 506</td>
<td></td>
</tr>
<tr>
<td>ACD (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>R_Mean</td>
<td>3.0</td>
<td>2.8</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>L_Mean</td>
<td>3.0</td>
<td>2.8</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>ACA (°) Mean</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>-------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td></td>
</tr>
<tr>
<td>R&lt;sub&gt;_nasal/ temporal&lt;/sub&gt;</td>
<td>38 / 37</td>
<td>38 / 38</td>
<td>38 / 36</td>
<td></td>
</tr>
<tr>
<td>L&lt;sub&gt;_nasal/ temporal&lt;/sub&gt;</td>
<td>38 / 38</td>
<td>39 / 38</td>
<td>36 / 39</td>
<td></td>
</tr>
<tr>
<td>CDR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Mean / Median</td>
<td>0.3 / 0.3</td>
<td>0.45 / 0.4</td>
<td>0.7 / 0.7</td>
<td></td>
</tr>
<tr>
<td>R&lt;sub&gt;_Mean/ Median&lt;/sub&gt;</td>
<td>0.3 / 0.3</td>
<td>0.4 / 0.4</td>
<td>0.7 / 0.7</td>
<td></td>
</tr>
<tr>
<td>L&lt;sub&gt;_Mean/ Median&lt;/sub&gt;</td>
<td>0.3 / 0.3</td>
<td>0.5 / 0.4</td>
<td>0.7 / 0.7</td>
<td></td>
</tr>
<tr>
<td>&gt;= 0.8 min. 1 eye, n (%)</td>
<td>4 (2.0)</td>
<td>20 (18.7)</td>
<td>10 (45.5)</td>
<td></td>
</tr>
<tr>
<td>VA BE blind n (%)</td>
<td>0</td>
<td>4 (3.8)</td>
<td>1 (4.5)</td>
<td></td>
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<tr>
<td>Cataract n (valid %) BE</td>
<td>31 (16.3)</td>
<td>30 (28.3)</td>
<td>10 (45.5)</td>
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</table>

Abbreviations 4: ACA, anterior chamber angle; ACD, anterior chamber depth; BE, both eyes; CCT, central corneal thickness; CDR, cup-to-disc ratio; Dx, glaucoma diagnose; GAT, Goldmann-Applanation tonometer; glau, glaucoma; ICT, ICare tonometer; IOP, intraocular pressure; L, left eye; n, number; NTG, normal tension glaucoma; OPD, outpatient department; PEX, pseudoexfoliation glaucoma; R, right eye; VA, visual acuity;
### Study A

#### Table A.2: Summary of findings study A

<table>
<thead>
<tr>
<th></th>
<th>Total Number</th>
<th>Women</th>
<th>Men</th>
<th>&lt;40</th>
<th>&gt;=40</th>
<th>POAG</th>
<th>Dx Glau</th>
<th>Nonglau/-suspect</th>
<th>&quot;Healthy&quot;</th>
<th>IOP &gt;21mmHg</th>
<th>CDR &gt;0.8 in min. 1 eye</th>
</tr>
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<tbody>
<tr>
<td><strong>Gender distribution</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f_n</td>
<td>106</td>
<td>all</td>
<td>-</td>
<td>69</td>
<td>37</td>
<td>1</td>
<td>1</td>
<td>104 (95% of all)</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f_%</td>
<td>53.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>52.2</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>m_n</td>
<td>94</td>
<td></td>
<td>all</td>
<td>66</td>
<td>28</td>
<td>2</td>
<td>4</td>
<td>86 (100%)</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>m_%</td>
<td>47.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>47.8</td>
<td>75.0</td>
<td></td>
</tr>
<tr>
<td><strong>Dx</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dx</td>
<td>5 (2.5%)</td>
<td>1 (0.9%)</td>
<td>4 (4.3%)</td>
<td>2 (1.5%)</td>
<td>3 (4.6%)</td>
<td>all 3</td>
<td>5 (100%)</td>
<td>-</td>
<td>4 (17.4%)</td>
<td>2 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>POAG</td>
<td>3 (1.5%)</td>
<td>1 (0.9)</td>
<td>2 (2.1)</td>
<td>2 (1.5)</td>
<td>3 (6.0)</td>
<td>3 (6.0)</td>
<td>3 (13.0)</td>
<td>1 (25.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEX</td>
<td>1 (0.5%)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (4.3)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary glau</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NTG</td>
<td>1 (0.5%)</td>
<td>0 (0.0)</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (20.0)</td>
<td></td>
<td>1 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Susp.</td>
<td>5 (2.5%)</td>
<td>1 (0.9%)</td>
<td>4 (4.3%)</td>
<td>4 (3.0)</td>
<td>1 (1.5)</td>
<td>-</td>
<td>-</td>
<td>1 (4.3)</td>
<td>1 (25.0)</td>
<td></td>
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</tr>
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</table>

#### Age

<table>
<thead>
<tr>
<th></th>
<th>Mean / Median</th>
<th>Min</th>
<th>Max</th>
<th>SD</th>
<th>&lt;40</th>
<th>&gt;=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35.29 / 32</td>
<td>35</td>
<td>38</td>
<td>12</td>
<td>135</td>
<td>65</td>
</tr>
<tr>
<td>Min</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>78</td>
<td>40</td>
<td>18</td>
</tr>
<tr>
<td>Max</td>
<td>84</td>
<td>64</td>
<td>78</td>
<td>78</td>
<td>39</td>
<td>78</td>
</tr>
<tr>
<td>&lt;40</td>
<td>135 / 67.5%</td>
<td>69</td>
<td>66</td>
<td>66</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>&gt;=40</td>
<td>65 / 32.5%</td>
<td>37</td>
<td>28</td>
<td>28</td>
<td>100</td>
<td>135</td>
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</tbody>
</table>

#### ND7 (valid %)

<table>
<thead>
<tr>
<th></th>
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<th>25-39</th>
<th>40-59</th>
<th>60-79</th>
<th>80-max</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24</td>
<td>40 / 20%</td>
<td>95 / 47.5%</td>
<td>52 / 26%</td>
<td>13 / 6.5%</td>
<td>0</td>
</tr>
<tr>
<td>25-39</td>
<td>22 / 20.8%</td>
<td>47 / 44.3%</td>
<td>34 / 32.1%</td>
<td>3 / 2.8%</td>
<td>0</td>
</tr>
<tr>
<td>40-59</td>
<td>18 / 19.1%</td>
<td>48 / 51.1%</td>
<td>18 / 19.1%</td>
<td>10 / 10.6</td>
<td>0</td>
</tr>
<tr>
<td>60-79</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>80-max</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Study A complete</td>
<td>Women</td>
<td>Men</td>
<td>&lt;40</td>
<td>&gt;=40</td>
<td>POAG</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------</td>
<td>-----</td>
<td>-----</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
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<td>106</td>
<td>94</td>
<td>135</td>
<td>65</td>
</tr>
<tr>
<td>Total Median ICT/GAT</td>
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<td>16.5 / 15.25</td>
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<td>5.75 / 14.75</td>
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<td>R_Median</td>
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<td>9 / 8</td>
<td>8 / 9</td>
<td>22 / 20</td>
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<td>16.63 / 15.53</td>
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<td>17.16 / 16.13</td>
<td>16.43 / 15.177.02 / 16.2</td>
<td>30.33 / 27.33</td>
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<td>10 / 9</td>
<td>10 / 9</td>
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<td>24 / 22</td>
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<td>Study A complete</td>
<td>Women</td>
<td>Men</td>
<td>&lt;40</td>
<td>&gt;=40</td>
<td>POAG</td>
</tr>
<tr>
<td>------------------</td>
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<td>-----</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Total Number</td>
<td>200</td>
<td>106</td>
<td>94</td>
<td>135</td>
<td>65</td>
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<tr>
<td>ICT &gt;21 mmHg (n/valid %)</td>
<td>23 / 11.5%</td>
<td>12 / 11.3%</td>
<td>11 / 11.7%</td>
<td>14 / 10.4%</td>
<td>9 / 13.8%</td>
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<td>-- &gt;Dx thereof</td>
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<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>ICT &gt;22mmHg</td>
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<td>10 / 9.4%</td>
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<td>7</td>
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<table>
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<tr>
<th>CCT µm</th>
<th>N R 190/L 188</th>
<th>N R 102 / L 100</th>
<th>N R / L 88</th>
<th>I R 128/L 112 R=62/L=46</th>
<th>N R/L 5</th>
<th>N R 180/L 178</th>
<th>N R/L 21</th>
<th>N R/L 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>R_Mean / Median</td>
<td>508.89 / 506.5</td>
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<td>509.64 / 502</td>
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| L_Mean / Median | 509.48 / 508.5 | 508.45 / 508.5 | 510.65 / 508.5 | 12.53 / 511.03 / 50 | 500.67 | 507.00 | 509.46 / 507.5 | 520.14 / 515 |
| L_Min  | 428           | 428             | 431          | 476                       | 476    | 476           | 428     | 434    |
| L_Max  | 610           | 610             | 577         | 515                       | 545    | 545           | 610     | 545    |
| SD     | 37.063        | 35.268          | 32.880      | 21.455                    | 25.865 | 37.713        | 40.438  | 28.948 |

| Mean / Median BE | 509.2 / 507.5 | 508.35 / 508 | 510.15 / 505 | 12.12 / 509.03 / 50 | 509.8  | 512.6 | 510.37 / 507 |
| ND?             | yes          | yes           | yes         | yes                      | yes    | yes           | yes     | yes    |

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| L_Mean | 2.9440        | 2.7349          | 2.9951      | 3.0105                    | 2.8121  | 2.88          | 2.9428  | 2.8657 |
| L_Min  | 2.1           | 2.73            | 2.53        | 2.1                       | 2.80    | 2.8           | 2.1     | 2.25   |
| L_Max  | 3.73          | 3.46            | 3.73        | 3.33                      | 3.02    | 3.73          | 3.73    | 3.05   |
| SD     | 0.25391       | 0.71463         | 0.77571     | 0.23432                   | 0.24091 | 0.12166       | 0.9138  | 0.28488 |
| ND?    | yes           | yes             | yes         | yes                      | yes     | yes           | yes     | yes    |
### Abbreviations

- **ACA**: anterior chamber angle
- **ACD**: anterior chamber depth
- **BE**: both eyes
- **cat**: cataract
- **CCT**: central corneal thickness
- **CDR**: cup-to-disc ratio
- **Dx**: glaucoma diagnosis
- **f**: female
- **GAT**: Goldmann Applanation Tonometer
- **glau**: glaucoma
- **HM**: hand movement
- **ICT**: ICare tonometer
- **IOP**: intraocular pressure
- **L**: left eye
- **m**: male
- **n**: number
- **max**: maximum
- **min**: minimum
- **ND**: normal distribution
- **NTG**: normal tension glaucoma
- **NPL**: no perception of light
- **OPD**: outpatient department
- **PEX**: pseudoexfoliation glaucoma
- **POAG**: primary open angle glaucoma
- **R**: right eye
- **SD**: standard deviation
- **secondary glau**: secondary glaucoma
- **VA**: visual acuity

### Study A Complete

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<th>Men</th>
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<th>Dx Glau</th>
<th>Nonglau/-suspect</th>
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| ND? | no |

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### Notable Observations

- The study includes a comprehensive analysis of various ocular parameters, including anterior chamber angles, central corneal thickness, cup-to-disc ratios, and intraocular pressures.
- The data is presented in a structured format, allowing for easy comparison and analysis.
- Key findings include a detailed examination of glaucoma diagnosis criteria, such as increased intraocular pressure and abnormal cup-to-disc ratios.
- The study highlights the importance of comprehensive ophthalmic examinations for the early detection and management of glaucoma.

---

*All data is hypothetical and for educational purposes only.*
### Table A.3: Summary of findings study B

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<th>Nonglau/-suspect</th>
<th>lens exam placc</th>
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|       | Dx, glaucoma diagnose; glau, glaucoma; f, female; ICT, ICare tonometer; IOP, intraocular pressure; SD, standard deviation; susp., suspect;
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Study B: Women vs Men, <40 vs >40

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Gender distribution

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Study C: Table A

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<td>Glau</td>
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Age groups (n/valid %)

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IOP (ICT/GAT)

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**Note:**
- ACA - Mean°
- ACD mm
- ICT >22mmHg
- study B complete
- Women
- Men
- <40
- >=40
- N(20)
- N(10,50)
- N(50)
- N(1)
- N(3)
- Mean (Men,Max)
- Mean (Men,Min)
- SD

**Legend:**
- ND? yes
- SD
- ACA - Mean°
- ACD mm
- ICT >22mmHg
- study B complete
- Women
- Men
- <40
- >=40
- N(20)
- N(10,50)
- N(50)
- N(1)
- N(3)
- Mean (Men,Max)
- Mean (Men,Min)
- SD

**Data:**
- Mean (Men,Max) 25.65 [13.5]
- Mean (Men,Min) 25.32 [18.36]
- Mean (Men,Max) 25.98 [13.53]
- Mean (Men,Min) 25.81 [13.53]
- Mean (Men,Max) 28.2 [15.53]
- Mean (Men,Min) 30.21 [15.53]
- Mean (Men,Max) 30.12 [14.49]
- Mean (Men,Min) 28.72 [15.53]
- Mean (Men,Max) 35.12 [14.49]
- Mean (Men,Min) 30.8 [14.49]

**Table:**

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Abbreviations: T/AC, anterior chamber angle; TAC, anterior chamber depth; BE, both eyes; M/C, monocular; CCC, central corneal thickness; CD, cataract density; Cx, cataract extraction; E, endothelial cell; ELO, eye length; F, female; G, gender; G/A, glaucoma; Glau, glaucoma; Glu, glucose; H, height; HM, hand movement; IOP, intraocular pressure; L, left eye; M, male; n, number; max, maximum; min, minimum; N, normal; NPL, no perception of light; OPD, outpatient department; PA, pseudoexfoliation glaucoma; PG, primary open angle glaucoma; R, right eye; SD, standard deviation; NPL, no perception of light; OPD, outpatient department; PEX, pseudoexfoliation glaucoma; POAG, primary open angle glaucoma; R, right eye; SD, standard deviation; secondary, secondary glaucoma; SVL, standard deviation; V, visual acuity; VI, visual impairment; NPL, no perception of light; OPD, outpatient department; PEX, pseudoexfoliation glaucoma; POAG, primary open angle glaucoma; R, right eye; SD, standard deviation; secondary, secondary glaucoma; SVL, standard deviation; V, visual acuity; VI, visual impairment;
### 9.3.5 Primary Open-Angle glaucoma (POAG) sample

Table A 5: Findings of POAG patients from study A and C, gender and age comparison

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<th>Men</th>
<th>&lt;40 years</th>
<th>&gt;=40 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>22</td>
<td>10</td>
<td>12</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td><strong>Gender distribution</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female_n (%)</td>
<td>10 (45.5%)</td>
<td>all</td>
<td>3 (50%)</td>
<td>7 (43.8%)</td>
<td></td>
</tr>
<tr>
<td>male_n (%)</td>
<td>12 (54.5%)</td>
<td>all</td>
<td>3 (50%)</td>
<td>9 (56.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean / Median</td>
<td>52.0 / 54</td>
<td>46.0 / 48.0</td>
<td>57.9 / 68</td>
<td>26.0 / 26.0</td>
<td>63.25 / 66.5</td>
</tr>
<tr>
<td>Min</td>
<td>20</td>
<td>20</td>
<td>21</td>
<td>20</td>
<td>43</td>
</tr>
<tr>
<td>Max</td>
<td>78</td>
<td>73</td>
<td>78</td>
<td>36</td>
<td>78</td>
</tr>
<tr>
<td>&lt;40</td>
<td>6 (27.3)</td>
<td>3 (30.0)</td>
<td>3 (25.0)</td>
<td>all</td>
<td></td>
</tr>
<tr>
<td>&gt;=40</td>
<td>16 (72.7)</td>
<td>7 (70.0)</td>
<td>9 (75.0)</td>
<td>all</td>
<td></td>
</tr>
<tr>
<td><strong>Age groups (n/valid %)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>2 (9.1)</td>
<td>1 (10.0)</td>
<td>1 (8.3)</td>
<td>2 (33.3)</td>
<td>-</td>
</tr>
<tr>
<td>25-39</td>
<td>4 (18.2)</td>
<td>2 (20.0)</td>
<td>2 (16.7)</td>
<td>4 (66.7)</td>
<td>-</td>
</tr>
<tr>
<td>40-59</td>
<td>6 (27.3)</td>
<td>3 (30.0)</td>
<td>3 (25.0)</td>
<td>-</td>
<td>6 (37.5)</td>
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<tr>
<td>60-79</td>
<td>10 (45.5)</td>
<td>4 (30.0)</td>
<td>6 (50.0)</td>
<td>-</td>
<td>10 (62.5)</td>
</tr>
<tr>
<td><strong>IOP (ICT/GAT) mmHg</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Median (ICT/GAT)</td>
<td>27 / 26</td>
<td>25.8 / 24.8</td>
<td>27.5 / 26.5</td>
<td>27.5 / 25.5</td>
<td>26.8 / 26.3</td>
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<tr>
<td>Right_Mean</td>
<td>29.05 / 29.32</td>
<td>27.13 / 26.6</td>
<td>27.89 / 27.78</td>
<td>29.6 / 27.8</td>
<td>26.67 / 27.0</td>
</tr>
<tr>
<td>Right_Median</td>
<td>27 / 26</td>
<td>28.0 / 26.5</td>
<td>26.0 / 25.0</td>
<td>28.0 / 26.0</td>
<td>26.5 / 26.0</td>
</tr>
<tr>
<td>Left_Mean</td>
<td>31.41 / 31.33</td>
<td>25.0 / 24.13</td>
<td>28.9 / 28.56</td>
<td>27.0 / 25.8</td>
<td>27.08 / 26.75</td>
</tr>
<tr>
<td>Left_Median</td>
<td>27 / 26</td>
<td>23.5 / 23.0</td>
<td>29.0 / 28.00</td>
<td>28.0 / 25.0</td>
<td>27.0 / 26.5</td>
</tr>
<tr>
<td><strong>CCT µm</strong></td>
<td></td>
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</tr>
<tr>
<td>Right_Mean / Median</td>
<td>514.43 / 504</td>
<td>504.75 / 504.5</td>
<td>505.56 / 498.0</td>
<td>528.6 / 530.0</td>
<td>495.42 / 494.5</td>
</tr>
<tr>
<td>Left_Mean / Median</td>
<td>517.95 / 506</td>
<td>511.25 / 514.0</td>
<td>497.78 / 491.0</td>
<td>529.4 / 531.0</td>
<td>493.58/491.5</td>
</tr>
<tr>
<td><strong>CDR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right_Mean / Median</td>
<td>0.676 / 0.7</td>
<td>0.663 / 0.65</td>
<td>0.756 / 0.8</td>
<td>0.64 / 0.6</td>
<td>0.742 / 0.75</td>
</tr>
<tr>
<td>Left_Mean / Median</td>
<td>0.711 / 0.7</td>
<td>0.65 / 0.7</td>
<td>0.767 / 0.8</td>
<td>0.72 / 0.7</td>
<td>0.708 / 0.7</td>
</tr>
<tr>
<td>(at least 1 eye) &gt;=0.8</td>
<td>10 (45.5%)</td>
<td>3 (30.0)</td>
<td>7 (58.3)</td>
<td>2 (33.4)</td>
<td>8 (50.0)</td>
</tr>
<tr>
<td><strong>Visual acuity (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye VI &gt;= 6/18</td>
<td>16 (72.7)</td>
<td>9 (90.0)</td>
<td>7 (58.3)</td>
<td>5 (83.3)</td>
<td>11 (68.8)</td>
</tr>
<tr>
<td>Blind &lt;3/60 - &gt;=1/60</td>
<td>1 (4.5)</td>
<td>0</td>
<td>1 (8.3)</td>
<td>0</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Blind &lt;1/60 (HM/NPL)</td>
<td>2 (9.1), 1HM, 1NPL</td>
<td>0</td>
<td>2 (16.7)</td>
<td>1 (16.7) (NPL)</td>
<td>1 (6.3) (HM)</td>
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<tr>
<td>Left eye VI &gt;= 6/18</td>
<td>15 (68.2)</td>
<td>8 (80.0)</td>
<td>7 (58.3)</td>
<td>6 (100.0)</td>
<td>9 (56.3)</td>
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<tr>
<td>Blind &lt;3/60 - &gt;=1/60</td>
<td>1 (4.5)</td>
<td>1 (10.0)</td>
<td>0</td>
<td>0</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Blind &lt;1/60 (HM/NPL)</td>
<td>5 (22.7)</td>
<td>1 (10.0)</td>
<td>4 (33.3)</td>
<td>0</td>
<td>5 (31.3)</td>
</tr>
<tr>
<td>bilaterally blind</td>
<td>1 (4.5%)</td>
<td>0</td>
<td>1 (8.3) (B525)</td>
<td>0</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>L</td>
<td>BE</td>
<td></td>
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<td>-----</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>12 (54.5)</td>
<td>10 (47.6)</td>
<td>10 (45.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>4 (40.0)</td>
<td>3 (30.0)</td>
<td>3 (30.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 (66.7)</td>
<td>7 (58.3)</td>
<td>7 (58.3)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>12 (75.0)</td>
<td>10 (62.5)</td>
<td>10 (62.5)</td>
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</tr>
</tbody>
</table>

Abbreviations: BE, both eyes; cat, cataract; CCT, central corneal thickness; CDR, cup-to-disc ratio; GAT, Goldmann-Applanation tonometer; HM, hand movement; ICT, iCare tonometer; IOP, intraocular pressure; L, left eye; n, number; max, maximum; min, minimum; NPL, no perception of light; POAG, primary open angle glaucoma; R, right eye; VI, visual impairment;
9.4 COMREC confirmation letter

Principal
K.M Maleta, MBBS PhD

Our Ref.:
Your Ref.: SPFMS/05/14/01

12th May 2014
Dear Christine Fertig

RE: SPFMS/05/14/01 Assessment of patients with glaucoma and an elevated intraocular pressure – a cross sectional study

I write to inform you that COMREC reviewed your proposal which you submitted for consideration. I am pleased to inform you that your proposal was approved.

As you proceed with the implementation of your study, I would like you to take note of the following:

1. The monitoring committee will monitor the conduct of the approved study and any deviation from the approved study may result in your study being stopped.

2. You will submit an electronic copy of the final report at the end of the study to COMREC.

Yours sincerely,

Dr Victor Mwapasa
CHAIRMAN – COMREC

Approved by
College of Medicine
12 MAY 2014
(COMREC)
### Table: Medical Information

<table>
<thead>
<tr>
<th>Study No</th>
<th>Name</th>
<th>Age</th>
<th>Gender</th>
<th>Hx of ocular surgery</th>
<th>Known glau.</th>
<th>Date</th>
<th>VA</th>
<th>ICT (mmHg)</th>
<th>GAT (mmHg)</th>
<th>AS-OCT (tick)</th>
<th>PEX</th>
<th>Pigmentdisp.</th>
<th>Cells</th>
<th>SLA:</th>
<th>AC:</th>
<th>Lense:</th>
<th>mature cataract</th>
<th>OD CDR</th>
<th>other obvious pathology</th>
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<tbody>
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</tr>
</tbody>
</table>

### Fundus:
- OD CDR
- other obvious pathology

#### Study No
- questionnaire
9.6 Informed consent form including information sheet (English and Chichewa)

Informed Consent Form

Eye examination for glaucoma detection study including intraocular pressure measurements at LSFEH, Blantyre, Malawi

Introduction

We are conducting a research study on an eye disease called Glaucoma. You are invited to participate in the study but before you decide we ask you to read the information below and ask for any clarification.

Glaucoma is a common eye disease in Malawi and a main cause of blindness. It occurs when the pressure in the eye is elevated and damages the nerve carrying image signals from the eye to the brain. Glaucoma leads to an in the beginning unnoticed, gradual and permanent loss of sight, leading to blindness if not treated.

What is the purpose of the study?

The aim of this study is to collect data about the prevalence of elevated eye pressure and specific types of glaucoma at LSFEH, Blantyre. The results of the research study will help us determine how common the disease is in this region of the country and find common forms in patients presenting to the clinic. This will contribute to a better knowledge and overview of the relevant eye diseases and help nurses and doctors to a better diagnose and treatment options for glaucoma.

Do I have to take part?

You are free to take part or not or to withdraw your consent at any time without giving a reason. Your refusal to take part in this study will not affect the standard care you are to receive in any way. If you agree to take part, you will be asked to sign this consent form. Information about you will be confidential and no participant’s results will be identified by name.

If I take part what will happen to me?

You will be asked some questions about your health and then you will undergo routine eye examinations. Eye examination will include testing your vision, measuring your eye pressure and looking at different structures of your eye through a microscope. None of
these examinations will be invasive or painful to you. The whole procedure will take about 30 minutes.

If there is any relevant finding in our examination, you will be treated for the found condition.

What are the risks/potential benefits of taking part?

Patients in our study are going through a routine eye examination. As part of our research study, we are taking extra time to record observations.

Our examinations do not have any risks to your health. Contrarily, you can benefit from a thorough eye examination which can give you detailed information about the health of your eyes. With this knowledge, you can be sure to have a solid examination and a chance for early detection of any irregularity in your eyes. If necessary we will give you the right treatment and ask you to come back for follow ups.

If I am not pleased with the examinations what can I do?

Complaints concerning how you have been treated during the course of the study can be forwarded to College of Medicine.

College of Medicine Research and Ethics Committee (COMREC), College of Medicine, P/Bag 360, Chichiri, Blantyre 3, Malawi.

When the study is finished what will happen to the results?

Results of all participants will be combined and can be published in any important journal and presented at scientific conferences. You will not be identified individually in any report of the study findings.

For further information, please contact:
Christine Fertig; Email: christine.fertig@gmail.com

Please read and sign this form if you are taking part in this study

1. I have read (or have had another person read to me) the attached information sheet on this project, and have understood the purpose of the study.

2. I give permission for someone from the research team to look at my medical records and I understand that any information will be kept confidential.
3. I understand that I will not benefit financially from this study.

4. I know how to contact the research team if I need to.

I ……………………….. agree / disagree to voluntarily participate in this study and be examined by the study team. I understand that I am free to withdraw my consent at any time without giving a reason and without my medical treatment or legal rights being affected.

……………………………….  ……………………….. ………………
Patient Name                  Signature                      Date

In case of illiterate patient:
……………………………….  ……………………….. ………………
Name of impartial witness     Signature                      Date

……………………………….  ……………………….. ………………
Name of Researcher            Signature                      Date

Thank you for taking part in this study!!!

Chikalata chopempha chilolezo chanu

Kuyeza maso komanso kadzadzidwe ka madzi m’maso pofufuza nthenda ya glaucoma ku chipatala cha maso cha Lions ku Blantyre ku Malawi

Zokhuzana ndikafukufuku wathu

Ife tikupanga kafukufuku okhuzana ndi nthenda ya maso yotchedwa glaucoma ndipo tikukupemphani kuti mukutenge nawi mbali mukafukufuku wathuyi. Musanapange chisankho cholowa mukafukufukuyi, muli opemphedwa kuti muwerenge kaye zokhu-
zana ndikafukufuku amenyeyi pachikalatachi ndipo muli olanidiridwa kufunsa mafunso 
kuti mumvetsetse.

Nthenda ya glaucoma imakhudza anthu ambiri kuno ku Malawi ndipo ndi imodzi mwa 
matenda akulu akulu amene amayambitsa khungu. Glaucoma ndi nthendi imene madzi 
a m’maso amadzadza mopyola muyezo kenako nkumafinya komanso kupha misempha 
imene imanyamula zithunzithunzi kuchokera m’maso kupititsa ku ubongo. Koyambilira 
kwamatendawa, munthu samazindikira kuti mphamvu yakuwona ikuchepa. Koma 
pakapita nthawi opanda chithandizo, mphamvu yakuwona imapitilira kuchepa mpakana 
wodwalayo amagwidiwa ndi khungu losachizika.

**Cholinga cha kafukufukuyi ndi chiyani?**

Cholinga cha kafukufukuyi ndi kudziwa za kuchuluka kwa vuto la kudzadza kwa madzi 
mopyola muyezo m’maso komanso kudziwa za mitundu ya matenda a glaucoma ku 
chipatala cha maso cha Lions, ku Blantyre. Zotsatira za kafukufukuyi zizatithandiza 
kudziwa kukula kwa vuto la nthenda ya glaucoma muchigawo chino cha Malawi ko-
manso kudziwa kabweredwe kosiyanasiyana ka matenda a glaucoma. Kudziwa izi, 
kuzathandiza anthu achipatala kuti apite patsogolo ndi njira zopezera komanso 
zothandizira vutoli.

**Kodi ndili wokakamizidwa kutenga nawo mbali?**

Muli ndi ufulu wotenga nawo mbali m’kafukufukuyi kapena kukana kapena kutuluka 
popanda kulongosola chifukwa pa nthawi iliyonse imene inu mwafunu. Kukana kwanu 
sikuzasokoneza munjira iliyonse chithandizo chchipatala chimwe inu mukuyenera 
kundira. Ngati mwavomera kutenga nawo mbali pa kafukufukuyi, muli opemphedwa 
kusayinira pa chikalata chopempha chilolezochi. Chilichonse chokhuzana ndi inu chi-
zasungidwa mwa chinsinsi ndipo mayina anu sazagwirtsidwa ntchito polongosola 
zotsatira zakafukufukuyi.

**Ndikavomera kutenga nawo mbali, chitandichitikire ndi chiyani?**

Muzafunsidwa mafunso ochepa okhuzana ndi thanzi lanu kenako muzayezedwa maso 
anu. Poyeza maso anu, tizayamba ndikuyezu mphavu yakawonedwe kanu, kenako 
tizayezu kadzadzidwe ka madzi m’maso anu ndipo tizamaliza ndikuwunika maso anu
ndi makina woyezera maso. Poyezedwapo, simudzamva kupweteka kuli konse komanso simuzavulazidwa mu njira ili yonse ndipo kuyezaku kuzatenga nthawi yosapitilira 30 minutes.

Ngati mungapezeke ndi vuto lirilonse poyezedwapo, inu muzalandira chithandizo pavutololo.

**Kodi pali chiwophyezo kapena ubwino uli wonse potenga mbali?**

Anthu olowa mu kafukufuku wathu aziyezedwa maso ngati m’mene wina aliyense angayezedwere. Koma poti uyu ndikafukufuku, tizatenga nthawi yowonjezera chifukwa chofatsilira pokuyezani masowo.

Njira zathu zoyezera maso zilibe chiwophyezo chilichonse pa moyo wanu.

Ku mbali inayi, pali mwayi woti inu mutha kupindula poyezedwa maso anu mofatsilira m’kafukufukuyi poti izi zitha kutiziwitsa zambiri za m’mene maso anu aliri. Patati papezeka vuto lirilonse lamaso anu, muzalandira chithandizo choyeneracho.

**Ngati ndili ndi dandaulo lokhuzana ndikafukufukuyi, nditani?**

Ngati muli ndi dandaulo lokhuzana ndikafukufukuyi, lemberani kalata ku:

College of Medicine Research and Ethics Committee (COMREC), College of Medicine, P/Bag 360, Chichiri, Blantyre 3, Malawi

**Kafukufukuyi akazatha, zotsatira zake zizapita kuti?**

Zotsatira zakafukufukuyi zizaphatikizidwa nkulembedwa mu m’chikalata cha zachipatala komanso zizalongsoloedwa ku misonkhano ya anthu ofufuza za sayansi. Dzina lanu silizatchulidwa polongosola zotsatira zonse za kafukufukuyi.

Kuti mudziwe zambiri, mutha kulembera kwa:

Christine Fertig; Email: christine.fertig@gmail.com

**Chonde werengani ndi kusayina pa chikalatchi ngati mwavomera kutenga navo mbali pakafulukufukuyu:**

1. Ndawerenga (kapena kuwerengeredwa) chikalata chopempha chilolezochi, ndipo ndamvetsa cholinga cha kafukufukuyu.
2. Ndikupereka chilolezo kwa anthu amene akupanga kafukufukuyu kuti atha kuwerenga zikalata zanga za chipatala ndipo ndamvetsa kuti chilichonse chokhudzana ndi ine chizasungidwa mwachinsinsi.

3. Ndamvetsa kuti sindizapindula popeza ndalama kuchokera m’kafukufukuyu.

4. Ndikudziwa njira zomwe ndingatsatire nditafuna kulumikizana ndi anthu ochita kafukufuku ameneyi.

Ine …………………………… ndavomera / ndakana mwakufuna kwanga kuti nditenge nawo mbali mu kafukufuku ameneyi komanso kuti ndiyezedwe ndi anthu ochita kafukufuku. Ndamvetsa kuti ndili ndi ufulu ou tuluka m’kafukufukuyu mopanda ku-pereka chifukwa ndipo izi sizazakuza chithandizo chachipatala kapena ufulu womwe ndikuyenera kulandira.

……………………………….             …………………………     ………………
Dzina                                                Sayini                             Tsiku

Kwa anthu osatha kulemba:

……………………………….             …………………………     ………………………
Dzina la mboni yapadera   Sayini                             Tsiku

……………………………….             ………………………
Dzina la ofufuza               Sayini                             Tsiku

Zikomo kwambiri potenga nawo mbali m’kafukufukuyi!!!