

**The intersection of Hypertension, Diabetes & HIV in Malawi:
Report on a research prioritization workshop**

3 - 4 July 2014, Zomba, Malawi

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Executive Summary

Participants from nine NGO and academic partner organizations, together with MOH representatives from programs including NCDs & Mental Health, HIV/AIDS, Research, and Community Health Services, along with two District Health Officers, met for two days to review the state of knowledge around the intersection of HIV, hypertension and diabetes. Priority research questions were rearticulated and clustered. Four working groups developed outlines for research proposals on (i) the burden of clinically important health outcomes (and mortality) related to hypertension and diabetes in Malawi, also looking at their association with HIV infection and its treatment, (ii) the most (cost-)effective means of screening for hypertension and diabetes at community, health centre and hospital levels, (iii) the effectiveness of current standard treatment guidelines for the treatment of hypertension among PLWHA taking ART, including determinants of adherence to behavioral and pharmacologic interventions, and (iv) determining the optimal model of care for the integration of NCD prevention, diagnosis & management with HIV care, beginning with a study of existing models of care and their outcomes as a prelude to an interventional study to evaluate a new model of care. Coordinating persons and other supporting group members were defined for each proposal, and a follow-up schedule was defined.

Objectives and methodology of the workshop

The aims of this workshop were:

- To review the state of knowledge and research in Malawi related to the intersection of HIV with Hypertension and Diabetes mellitus
- To identify the priority research questions related to prevention, diagnosis and treatment of Hypertension and Diabetes (and related clinical events) among Persons Living with HIV/AIDS
- To outline 3-5 research proposals based on the priority questions, and to identify collaborating partners from among the participants

Participants were drawn from a variety of organizations working in Malawi on non-communicable diseases and/or HIV, representing non-governmental organizations, academic health partnerships, civil society organizations and the Ministry of Health of Malawi. (*A full list of participants is provided in Appendix B.*) The workshop was hosted by **Dignitas International**.

The **Workshop Planning Committee** included: Dr Theresa Allain (former Head of Department of Internal Medicine, College of Medicine, Blantyre), Dr Moffat Nyirenda (College of Medicine, Blantyre & Karonga Prevention Study), and Dr Beatrice Mwangomba (NCD Program Manager, Ministry of Health, Lilongwe).

Presentations were made on the epidemiology of non-communicable diseases (with particular reference to hypertension and diabetes in Africa, and in Malawi specifically), on the contribution of HIV infection to cardiovascular disease, and on the relationship of

antiretroviral therapy with hypertension and diabetes. The **National NCD Prevention Strategy**, including the Action Plan, was summarized and discussed.

Representatives of various participating NGOs presented the **NCD-related activities** taking place in their district programs. A civil society (and patient) perspective was provided by the President of the Diabetes Association of Malawi. A presentation was provided on the application of cost-effectiveness analysis to interventional research, as could be applied to NCD-related interventions.

With reference to the **Malawi national research priorities for hypertension and diabetes** and other relevant literature, participants identified specific research questions of interest reflecting their individual and organizational perspectives. These questions were clustered thematically and participants identified the question (or cluster of questions) that they wished to develop into a research proposal outline. This resulted in four work groups developing four research proposal outlines that were discussed in plenary. Responsible persons, and supporting group members, were identified from within each work group for further development of the research proposals in the weeks and months after the workshop, and a timeline was defined for next steps.

The detailed final workshop programme is provided in Appendix A

The current state of knowledge

The Epidemiology of NCDs was described by Moffat Nyirenda, beginning with a description of the situation in sub-Saharan Africa from a global perspective. Malawi is one of many countries in the region facing overlapping epidemics of HIV and NCDs. Unfortunately, Africa has the highest age-standardized death rates from NCDs in the world.

The Malawi STEPS survey (2009) provided more country-specific data than had been previously available. The overall prevalence of hypertension (HT) of 32.9%, and 93.3% of people with hypertension were unaware they had it. There are age-related and regional variations in the prevalence of hypertension in Malawi.

The NCD epidemic in Africa has some unique features: the transition to a greater burden of NCDs has occurred earlier than expected, and rapidly; it is affecting younger people and it is not associated with affluence. HIV infection and the effects of antiretroviral therapy are among the suspected drivers of the NCD epidemic in Africa. HIV-infected persons in Malawi are more likely to have hypertension, diabetes mellitus (DM) and hyperlipidemia. People with HIV are living longer due to more effective application of antiretroviral therapy but they are at risk for a variety of non-AIDS related complications.

Overall, these findings imply the need to better understand the nature & natural history of hypertension and diabetes in Malawi, to assess the clinical impact (complications) of these conditions, and to develop interventions to prevent these conditions and to best care for individuals with them.

Information on the PowerPoint slide set used in this presentation is provided in Appendix C.

A folder containing 6 papers based on the Malawi STEPS Study is also provided in Appendix C.

The contribution of HIV to cardiovascular disease (CVD) was presented by Christine Kelly.

Although determining the prevalence of diabetes among HIV-infected persons is difficult, it is thought that the risk of type 2 diabetes is increased by 2-4 fold over HIV-uninfected persons. Immune activation and the presence of co-infections (such as TB) may also play a role. Both diabetes and hypertension are associated with a longer duration of HIV infection and a lower nadir CD4 count. Hypertension may be associated with elevations in markers of bacterial translocation. Traditional markers of cardiovascular risk are differently distributed in HIV-infected persons than in the HIV-uninfected. In a study of incident cardiovascular disease events among HIV-infected persons, the most important attributable risk factors were age ≥ 42 years, hypertension, tobacco smoking & CD4 count < 500 cells/ μ L. It appears that among people with advanced HIV there is evidence of abnormalities in endothelial function both at baseline and post-ART initiation.

The PowerPoint slide set used in this presentation is provided in Appendix C.

The association of antiretroviral therapy (ART) with hypertension and diabetes was presented by Joep van Oosterhout.

It is difficult to distinguish the effects of HIV from those of ART. More widespread use of ART has resulted in an ageing population of patients with a consequently longer duration of exposure to traditional risk factors for HT, DM and CVD. A variety of multi-drug ART regimens are used to treat HIV and there have been no studies directly comparing regimens regarding HT, DM or CVD as main outcomes.

Western studies have shown a *short term* beneficial effect of ART has been documented, thought to result from reduced inflammation associated with suppression of HIV replication. They have also shown a *long term* harmful effect of ART. The most recent systematic review and meta-analysis of 27 studies found that PIs and Abacavir were associated with increased CVD risk. Although there is no evidence that ART increases the risk of developing HT, the prevalence of HT is high among ART patients, and the impact of HT or CVD risk may be greater in this group. ART is associated with increased risk of type 2 DM, which often develops in the context of the 'metabolic syndrome' and/or lipodystrophy.

There is much less information from Africa but a systematic review published in 2013 (Dillon DG et al; International Journal of Epidemiology) showed no association between ART and HT. It also showed that ART was associated with lower HbA1c – which is inconsistent with Western studies; HbA1c may not be the best measure of glycemic status for Africans. There are no studies on the association of ART with cardiovascular disease (CVD) endpoints in Africa.

In contrast to the systemic review cited above, the Malawi STEPS survey found that, among ART patients in Blantyre, the prevalence of HT was 45.9% compared to a Malawi general population prevalence of 32.9%. In a population of patients treated with Triimmune30 at Queen Elizabeth Hospital (Blantyre) the prevalence of HT increased from 3% at month 12 to 16% at month 24.

The PowerPoint slide set used in this presentation is provided in Appendix C.

Programmatic and research activities related to hypertension, diabetes & HIV in Malawi

The **National Action Plan for the Prevention & Management of Non-Communicable Diseases in Malawi (2012-2016)** was summarized by Beatrice Mwangomba. With regard to hypertension and diabetes, the Action Plan focusses on awareness raising and health lifestyle promotion (e.g., diet, smoking, physical activity) and related institutional policies aimed at reducing exposure to known risk factors. She cited some pressing health system requirements, including:

- A need for effective triage given the current failure to adequately screen for early diagnosis and treatment of HT
- Development of a ‘chronic care clinic’ model designed to ensure systematic follow-up and better continuity of care
- Continued development of an Monitoring & Evaluation (M&E) plan and tools (an NCD master card is currently in development)
- Looking for alternate providers for NCD-related counselling, and possibly involving Health Surveillance Assistants (HSAs), given that nurses are not available for this.

The MoH NCD Action Plan, the Final CVD, DM, CRD Protocol, and the draft NCD Master Card are provided in Appendix D.

The **Malawi Epidemiology and Intervention Research Unit (MEIRU)**, is the new name for the Karonga Prevention Study (KPS) since the addition of a new site in Lilongwe in 2012. MEIRU, led by Moffat Nyirenda, is a partnership between the Malawi College of Medicine (COM), the London School of Hygiene and Tropical Medicine (LSHTM) and the Malawi Ministry of Health. The main focus of their work is on surveys to accurately determine the burden and driving risk factors for NCDs in Karonga and Lilongwe. They will recruit 18,000 and 23,000 adults in Karonga and Lilongwe, respectively, (7000 recruited so far) each of whom will undergo a detailed interview (regarding lifestyle and medical risk factors), examination with biophysical data recording, and a detailed laboratory analysis. They will also be offered HIV testing. These surveys will lead to the identification of cohorts to provide a better understanding of the phenotype of disease – for example, the nature and natural history (patterns of complications) of hypertension in Malawi. Data will also be contributed to genomic studies in sub-Saharan Africa as genetic determinants may play an important role in NCD susceptibility. Early data from the surveys are already sufficient to plan intervention studies, for example regarding reduction of salt consumption, and to prevent progression from pre-diabetes to overt diabetes. MEIRU is also committed to research capacity building and aims to create a centre of excellence for training and research.

A summary of MEIRU and its activities is provided in Appendix D.

Lighthouse Trust (Lilongwe) was represented by Joe Gumulira, who presented their approach to screening and management of HT. They support two tertiary referral ART clinics, with a combined cohort of 25,000 patients (23,500 of which are on ART).

Task shifting is planned such that the Patient Attendant at the vital signs station will be responsible for routine screening; the Electronic Medical Record (EMR) will be enhanced to prompt BP screening, record BP electronically and aid management.

They propose to begin by screening patients >50 year of age; once they are all screened all those >40 years of age, and so on. The rationale is that older patients are more likely to have HT, and also at higher risk of CVD at a given BP.

Standard treatment guidelines will be used but there is concern regarding interactions between calcium channel blockers (CCB) and ART. 96% of their patients are on NNRTIs which reduce CCB levels, and the other 4% are on PIs which significantly increase CCB levels, so the Lighthouse algorithm has been refined to reflect this:

Malawi Standard Treatment Guidelines	Lighthouse Algorithm
Loop diuretic	Hydrochlorothiazide 25 mg OD
Calcium-channel blocker (CCB)	Enalapril 10 mg OD (ACE-I)
Angiotensin Converting Enzyme Inhibitor (ACE-I)	Amlodipine 5 mg OD (CCB)
Beta Blocker	Refer to senior clinician re: dosages ACE-I, CCB
	Atenolol 50-100 mg OD (Beta Blocker)

For further details see Appendix D.

Chembe Kachimanga, representing **Partners in Health**, described NCD integration efforts in Neno District, where PIH works with the MoH. They support two clinics, a Chronic Care Clinic, and a Palliative Care & Cancer Clinic. The Chronic Care Clinic has 2 sites with 497 active patients in Apr-June 2014 (213 HT, 41 DM, 110 asthma, 122 mental health, the remainder other conditions or multiple diagnoses). The clinic runs with a multi-disciplinary team: 4 clinicians, pharmacists, procurement technician and EMR team. NCD-HIV integration activities include:

- HIV counselling & referral for testing during CCC visits (intake form has HIV/ART questions)
- Education on common chronic diseases, and screening for HT, at ART clinics & HIV community events
- Education of village health workers (who have traditionally focused on HIV) on NCDs.
- Leveraging defaulter tracing systems from the HIV program

Major next steps:

- Pilot MoH tools (master cards) in Neno District
- Decentralize services to Health Centres (propose to integrate into existing ART program to combine transport, scheduling and human resources)
- Continue and expand community education and screening

For further details see Appendix D.

The **EQUIP project** in Mzuzu, supported by **Partners in Hope**, was described by Colin Pfaff.

A study undertaken to determine the prevalence of HT and pre-HT among ART clinic patients found:

- HT prevalence 31%, pre-HT 32.9%, based on a single measurement; male sex & age >40 both associated with higher odds of HT
- Only 5.5% of those with BP >139/89 reported a known diagnosis of HT & had previous or current treatment

Another study was undertaken to assess the capacity to provide HT and DM services at 25 health centres and 5 hospitals in Nkhata Bay & Mzimba North Districts, and specifically to describe the organization of management support and service delivery, and to assess human resource capacity, availability of diagnostic equipment and medication, laboratory capacity, information captured in routine health information systems. Findings included:

- Only 40% of ART-NCD patients received treatment from the same provider on the same day; 43% had treatment in different rooms but on the same day
- Only 10% of Medical OPDs measured BP on every patient; only 3% of ART clinics did so
- 84.5% of clinicians were *not* trained in NCDs; 83% of nurses were *not* trained in NCDs
- Medication availability at hospitals for HT and DM treatment varied markedly by agent
- At health centres most relevant drugs are not reliably available, except hydrochlorothiazide and 50% glucose injection
- They concluded that some integration is happening already, with NCD clinics at some hospitals but screening is very poor. Training needs are great, including diet counselling and there may be potential for task shifting. Drug & equipment needs are most pressing at health centres.

For further details see Appendix D.

A community advocacy (and patient) perspective on DM was provided by Mr. Timothy Ntambalika, President of the **Diabetes Association of Malawi**, which is affiliated with the World Diabetes Association. He described a 2-year project aimed at increasing awareness of DM:

- A (DM) patient committee was struck at every district hospital, to help educate patients and their guardians on treatment, diet, exercise, etc.
- Education on DM takes place at village level, with some support for screening activities
- Challenges include :

- Insufficient diagnostic (glucose test strips) and medication supplies
- Insufficient budget for transport
- Mass media messages (e.g., radio) are expensive and would need to involve 12-15 stations to provide high exposure
- Health personnel trained on DM are often transferred away from health facilities

Levison Chiwaula from Chancellor College, Zomba, described the way that **Cost-Effectiveness Analysis** (CEA) could be applied to interventional research on NCDs.

- CEA is important because we face absolute scarcity, and because there is an opportunity cost related to the use of resources for one intervention over another
- CEA allows us to compare interventions based on cost benefit ratios
- Decisions are typically made using an Incremental Cost-Effectiveness Ratio (ICER): $\text{Cost A} - \text{Cost B}$, over $\text{QALY A} - \text{QALY B}$ (where QALY = quality-adjusted life year)
- Economic studies of NCDs could include cost analysis of prevention & treatment of NCDs, CEA of different interventions, and/or equity analysis – by asking who is accessing care.

Information on obtaining the slide set used in this presentation is provided in Appendix D.

Four Research Proposals and Follow-Up Plans

Within the scope of the Malawi MoH National Health Research Agenda 2012-2016, workshop participants developed a list of research questions in the areas of epidemiology, clinical effectiveness, health systems, and patient perceptions & health-seeking behavior. *A full list of these research questions is provided in Appendix E.* Participants clustered into four work groups for the purpose of research proposal development on the questions they felt deserved priority. Four proposal outlines were produced, as described below. *Detailed notes on each proposal are provided in Appendix F.*

(1) The burden of disease associated with Diabetes and Hypertension in Malawi

What is the morbidity and mortality associated with diabetes and hypertension in Malawi, and how does it differ according to HIV status? These questions could be addressed in the short to medium term through a cross-sectional prevalence study of complications of HT and DM, using and adapting existing clinical information systems and master cards. A related, longer term cohort study could determine the incidence of clinically important endpoints, and the prevalence of factors related to them, and could be used to validate surrogate markers and risk assessment tools.

Next Steps: Mulinda Nyirenda (QECH & COM) will coordinate further development of this research proposal, with support from Beatrice Mwangomba (MoH), Christine Kelly (MLW), Sumeet Sodhi (DI) and Monique van Lettow (DI), and expert advisory support from Moffat Nyirenda (KPS).

(2) Screening for Diabetes and Hypertension

What is the most effective method to screen for diabetes and/or hypertension? A cross-sectional prevalence study could be used to compare at least 2 different screening methods, each using different criteria for screening, and comparing these methods to screening all adults, in order to determine which method yields more cases for the number screened, which is most sensitive for detection of severe disease, and which is most cost-effective.

Next Steps: Damson Kathyola (MoH) will coordinate further development of this research proposal, with support from Colin Pfaff (Partners in Hope), Chembe Kachimanga (PIH), and George Bello (MoH).

(3) The Effectiveness of Treatment for Hypertension among PLWHA

How effective are the Malawi standard treatment guidelines for the treatment of hypertension among people on ART, and what factors influence adherence to treatment? These questions could be addressed through a prospective cohort study enrolling ART patients who are newly

diagnosed with hypertension and following them for 12 months. This study aims to investigate the role of lifestyle changes as well as pharmacologic therapies.

Next Steps: Joep van Oosterhout (DI) will coordinate further development of this research proposal, with support from Boniface Banda (CHC), Blackson Matatiyo (NAC), and Jonathan Kalua (MoH Neno).

(4) The Model of Care for integration of NCD with HIV care

Which model of care is most effective for detecting and managing hypertension and diabetes among HIV-infected persons in both clinical and programmatic terms? A formative study is proposed to inform the later development of a 'Model of Care' cluster randomized trial. The formative work is proposed as a retrospective, mixed methods study which would comprehensively describe existing models of NCD/HIV integrated care, and report on the clinical and programmatic outcomes of those models.

Next steps: Adrienne Chan (DI) will coordinate further development of this research proposal, with support from Zengani Chirwa (MoH), Tithi Dzewela (MoH), Sumeet Sodhi (DI).

Other follow-up plans & suggestions:

- This report should be shared at the NCD Knowledge Translation Platform and should also be disseminated to other interested persons and organizations that were not present at the workshop.
- A small committee of 3-4 members was proposed to monitor progress and to generate future ideas for NCD-related collaborative work.
- A mailing list should be set up to keep interested persons and organizations up to date on NCD-related developments.
- Coordinating persons for each of the four proposals to be developed should provide a progress update to other workshop participants by 15 September 2014.
- It was requested that Prof Moffat Nyirenda provide expert review of near-final versions of the proposals being developed, to the extent that he available to do so.

Appendix A:

Final Programme - Research Prioritization Workshop: HIV, Hypertension & Diabetes

DAY 1 (THU 3 JULY) 08:30–16:30

Time	Topic	Methodology	Key persons
8:30-8:45 (15m)	Welcome & Introduction	DI welcome Overview agenda Participant Intros	J van Oosterhout, R Bedell
8:45-9:30 (45m)	Epidemiology of HT & DM in Malawi: STEPS study & other related studies <ul style="list-style-type: none">• Clinically important endpoints• Modifiable risk factors	Didactic + Q	M Nyirenda KPS
9:30-10:15 (45m)	HT/DM in PLWHA: effects of disease, and of ART	Didactic + Q	C Kelly MLW J van Oosterhout
10:15-10:30 (15m)	Break		
10:30-11:00 (30m)	National Prevention Strategy & commentary	Didactic + Q	B Mwangomba MOH
11:00-12:30 (90m)	Current practices re: HT & DM in clinical settings <ul style="list-style-type: none">• Participant experiences• Models of care• Evaluations Ongoing research on NCD, with particular reference to PLWHA	Presentations by participants Didactic + Q [Describe programs & related research]	C Pfaff Partners in Hope C Kachimanga PIH J Gumulira Lighthouse S Sodhi / JvO DI Other M Nyirenda KPS
12:30-13:15 (45m)	LUNCH		
13:15-13:45 (30m)	What do we know about community perspectives and awareness-raising on HT & DM, and how to research them?	Didactic + plenary discussion [Film clips from Tom Gibb]	T Ntambalika DAM + facilitator RB
13:45-14:30 (45m)	Incorporating cost- effectiveness analysis in interventional research	Didactic + Q	Levison Chiwaula ChanCo
14:30-14:45 (15m)	Break		
14:45-16:15 (90m)	From knowledge gaps to research questions`: <ul style="list-style-type: none">• Epidemiology• Population level interventions	Plenary discussion	RB chairs With support from DI facilitators

	<ul style="list-style-type: none"> Clinical interventions 		
16:15-16:30 (15m)	Quick recap of DAY 1		RB
16:30	END of DAY 1		

DAY 2 (FRI 4 JULY) 08:00-14:30

Time	Topic	Methodology	Key persons
8:00-8:15 (15m)	Intro to DAY 2 agenda		RB
8:15-10:00 (105m)	Translation of research questions into study outlines: definition of study population, methodology & time frame(continues)	3-4 Small work groups (≥ 4 members each) working in parallel	Each group to assign presenter/rapporteur; DI facilitators will support process
10:00-10:15 (15m)	BREAK		
10:15-10:45 (30m)	...(continued) Translation of research questions into study outlines: definition of study population, methodology & time frame	3-4 Small work groups (≥ 4 members each) working in parallel	Facilitators will assist where required: groups prepare to present
10:45-12:00 (75m)	Work groups feedback to whole group with discussion and input to improve proposals	Short presentation followed by plenary discussion, for each work group in turn	RB & rapporteurs for each group
12:00-12:45 (45m)	LUNCH		
12:45-13:45 (60m)	Collaborative research (& funding) opportunities among participants and their organizations/institutions	Continued as above	RB chairs plenary;
13:45-14:15 (30m)	Defining next steps for each proposal & key persons	Plenary discussion	RB chairs
14:15-14:30 (15m)	Recap of Workshop output & dissemination process	Plenary discussion	RB chairs
14:30	END of WORKSHOP		

Note: +Q means time for questions/brief discussion, after the presentation

Appendix B

A **List of Workshop Participants** with affiliations and contact information is provided in an Excel file with the file name

- **APX B Participants.xls**

Appendix C

Slide sets for 2 presentations on the current state of knowledge are provided in separate PowerPoint files with the file names

- **APX C CKelly.ppt**
- **APX C JvOosterhout.zip**

Another slide set **APX C MoffatNyirenda.ppt** is too large to attach to this report (>10 MB) but is available upon request.

In addition, 6 papers from the Malawi STEPS Study are provided in a zipped folder with the file name

- **APX C STEPS papers.zip**

Appendix D

The MoH NCD Action Plan, the Final CVD, DM, CRD Protocol, and the draft NCD Master Card, and a summary of MEIRU and its activities, are provided in a compressed folder with the file name

- **APX D MoH & MEIRU documents.zip**

Slide sets for presentations on programmatic & research activities in Malawi are provided in compressed folder with the file name

- **APX D NCD-HIV programs & research.zip**

This compressed folder contains the files **APX D Lighthouse.ppt**, **APX D PIHealth.ppt** -- *note that photos and a map were removed to decrease the size of this file, and APX D PIHope.ppt*

The slide set used to accompany the presentation on **Cost-Effectiveness Analysis** is >1 MB in size even if compressed so it will not be routinely attached to this report but is available upon request.

Appendix E

Research questions generated by workshop participants

Within the national research priorities of the MoH regarding HT and DM, participants generated the following list of research questions of interest to themselves and their organizations/institutions. These have been reorganized in relation to the NCD research themes that emerged; the work group that chose each issue for proposal development is indicated:

Epidemiology:

- What is the incidence/prevalence of morbidity & mortality related to complications of DM & HT? [Group 1]
- How valid are internationally developed CV risk measurement tools to the Malawian population (including HIV+ patients in particular)? [Group 1]

Clinical effectiveness:

- What is the most effective method to screen for DM and/or HT (in order to detect the patients at highest risk for HT & DM and related clinical endpoints)? [Group 2]
- What is the most effective way to counsel on lifestyle, including dietary modification (who, where, how frequently, with what content, with which modalities)? [Group 3]
- How effective are the Malawi standard treatment guidelines for HT & DM when applied to HIV+ patients? [Group 3]
- What is the most cost-effective means of monitoring DM in Malawi?

Health system issues:

- What are the existing models of care for HT & DM in Malawi? [Group 4]
 - a. What is the most effective means of linking newly diagnosed patients with DM and/or HT to care/treatment?
 - b. What is the actual availability of effective treatments for HT & DM in HC in Malawi?
 - c. What are the knowledge & skills of clinicians in HC and hospitals regarding diagnosis & treatment of HT & DM?
- What is the best M & E framework for evaluating programs HT & DM (prevention, diagnosis, treatment)? [Group 4]

Perceptions & health-seeking behaviours:

- What is the most effective method for awareness rising for HT & DM (in terms of knowledge, health-seeking behavior)? [Group 2]
- How do people understand a diagnosis of HT or DM, and what responses do they have to these diagnoses?
- Which factors influence successful lifestyle change in response to HT & DM (or risk of these conditions)?

- Is integration of NCD care with HIV+ patients acceptable to HIV- patients?

Appendix F

Detailed Study Proposal Outlines

(1) Group 1 Study question(s):

- **What is the morbidity and mortality associated with Diabetes and HTN in Malawi?**
 - Does this differ according to HIV status?

Rationale:

- The global burden of disease data is limited in Malawi and further research is needed to inform this.
- We currently don't know mortality rates and morbidity associated with HTN and diabetes in Malawi. It is important to have a baseline.

Data Sources & Methods

- Measure complications among community members, outpatients & hospital patients
- HMIS has data on HTN, diabetes, heart disease, NCDs (MoH has given HMIS a list to break down NCDs but this hasn't been incorporated yet); Baobab systems are another opportunity
- Connect clinical outcomes with HTN and diabetes
 - Need to link OPD and inpatient to trace patients through the system on EMR in central hospitals
- Know the denominator
 - Can use master cards from Southern regions (It may be easier to answer this, for example, in Neno District rather than somewhere central like QEH where we don't know where people are coming from)
- This will be more challenging for HTN
 - Possible to adapt urban data to look for people who have regularly attended follow-up; could link this with private hospitals
 - Could look at other cohort studies regularly recording BP
 - Still possible to use current data as a starting point

Study Design(s)

- Short/medium term: Cross-sectional prevalence study of complications
 - Use DM master cards to identify patients; collect data on history of clinical events, complications and HIV status
 - Study the prevalence of HT and DM in ART clinics in the same districts, or do screening in an ART clinic for 3 months
- Long term: Cohort study

- Determine the incidence of complications and factors related to the development of clinical events
- Further questions to incorporate are:
 - Validation of surrogate markers to make future research more feasible
 - Design & validation of risk assessment tools to target resources to the most 'at risk' populations

(2) Group 2 Study Question(s):

- **What is the most effective method to screen for DM and/or HT?**
- Which system yields the largest number of those affected per person screened?

Rationale:

- We don't know if it is more effective to target screening, or screen everyone
- It may be useful to compare two different targeted screening systems with screening everyone

Outcomes of interest:

- Total number of cases detected (per population)
- Number of cases with severe disease detected
- Cost-effectiveness of the screening method
- Sensitivity of the targeting criteria to detect severe disease
- Proportion of those screened (and found to have disease) linked to care

Study design: Cross-sectional prevalence study

Study population, sites & sampling:

- Screen everyone sites: all adults >24 years
- Targeting criteria to be refined: one or more of age, BMI, waist circumference, etc.
- Community-based: cluster sampling with household survey
- Facility-based: consecutive patients (meeting criteria, if any applied)

(3) Group 3 Study Question(s):

- **How effective are the Malawi Standard Treatment Guidelines for HT when applied to people on ART?**
 - How effective are life style changes for mild hypertension when applied to people living with HIV?
 - What are factors contributing to adherence to life style changes, hypertension drugs and HAART?

Rationale:

- We do not know the prevalence of HT or factors associated with HT among people on ART
- We do not know the effectiveness of current HT treatment for HIV infected persons on ART

Outcomes of interest:

- Levels of adherence
- Prevalence of pre-defined BP control targets
- Association between various factors and BP

Study design: Prospective cohort study

Study population, sites & sampling:

- Adult PLHIV on ART with newly diagnosed hypertension
- Sites will be ART clinics in both rural and urban settings, in all 5 health zones in Malawi
- Sampling method: Stratified random sampling of ART clinics (study participants will be enrolled based on specified inclusion/exclusion criteria to be developed at a later stage).
- Clinical follow-up of study participants for 12 months
- Data required: Quantitative (biophysical) and qualitative

Research skills required:

- Epidemiological skills
- Clinical skills
- Social science skills
- Statistical Skills

Materials required:

- BP Machines
- Weighing scales
- Laboratory resources (human and material)

Cost & funding considerations: US\$300,000 (subject to further review)

(4) Group 4 Study Question(s):

- **What is the preferred Model of Care: how do we integrate NCD (HT/DM) with HIV care?**
 - What are the existing NCD/HIV Integration models in Malawi?
 - Which model is
 - Most effective at optimizing program outcomes?
 - Detecting NCDs in HIV patients
 - Following up and managing NCDs in HIV patients

- Detecting HIV in NCD patients
 - Most effective at impacting clinical outcomes?
 - Most cost-effective and feasible for scale-up?

Formative work:

- Identify existing models of NCD and HIV Integration
 - Also learning lessons from HIV scale up of chronic disease management
- Evaluate existing models of NCD and HIV Integration
 - Retrospectively through model-specific data gathering
 - Operations research prospectively through implementation of MOH M & E tools being developed

Goals of formative work to inform a 'Models of Care' intervention:

- Cluster randomized trial to answer:
 - How do we integrate NCD (HTN and DM) and HIV Care?
- Informed design of interventions from formative work
- Endpoint/Outcomes:
 - To identify and detect clients with NCDs within the HIV care system
 - Manage and follow up clients with NCDs within HIV care system
 - Identify and detect HIV clients in NCD services
 - One stop shop vs. partial integration
 - Intersection of TB with HIV and DM? (role?)
 - Where should HIV clients be managed (in NCD system or within HIV)

Methods (for the pragmatic, formative research phase):

- Retrospective mixed methods, with quantitative and qualitative components
- Study population and location:
 - Primary, secondary and tertiary level health facilities
 - Adult patients
 - HCWs and Key Informants (program perspective)
 - Include Lighthouse, PIH /Neno, Area 25 KPS, Equip/ Partners in Hope, Kasungu DHO, Dr. T. Allain's work in Southern region and QECH
- Sampling method: purposeful
 - Number of sites: comprehensive (identified in collaboration with Beatrice Mwangomba/MoH NCD Program)
- Time frame 1 year-1.5 years:
 - 2-3 months proposal writing and ethics
 - 4-5 months data collection
 - 3-4 months analysis and write-up

Data requirements:

- Description of Models:

- HCWs, cadre, roles, training, task shifting
- Days clinic open, physical space, patient flow
- Equipment and supplies (stock outs, availability)
- Degree of integration
- SOPs
- Data collection tools
- Pt. support groups and community engagement
- Outcomes of models:
 - Program outcomes
 - Quantitative: Uptake; proportions of patients accessing both services
 - Qualitative: patient satisfaction, HCW opinions
 - Clinical outcomes: biophysical data and measurements, laboratory data

Funding & costing: consider CDC, USAID, CIHR or I-TECH

Appendix G

Abbreviations

ART	Antiretroviral therapy
COM	Malawi College of Medicine
CRD	Chronic respiratory disease
CVD	Cardiovascular disease
DM	Diabetes mellitus
EMR	Electronic Medical Record
HCW	Health Care Worker(s)
HSA	Health Surveillance Assistant
HT	Hypertension
LSHTM	London School of Hygiene and Tropical Medicine
MEIRU	Malawi Epidemiology and Intervention Research Unit
MLW	Malawi-Liverpool-Wellcome Trust Clinical Research Programme
MOH	Ministry of Health
M&E	Monitoring & Evaluation
NCD	Non-communicable disease(s)

QECH Queen Elizabeth Central Hospital, Blantyre