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Type 2 Diabetes in Rural Uganda:
Prevalence, risk factors, perceptions and
implications for the health system

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Cover Photo: Choice competing with the lack of it

Photo Credit:
Fred Inklaar, Fruit market, Uganda
FPRI-Images, Market in Malawi
Amy the Nurse, Grocery store, Kenya
Carsten ten Brink, Mix them yourself if you like

To my beloved brother, Michael 'Mitchell' Kyambadde (1977-2014);
Gone too soon….

"Here is a community where obesity signifies success. High risk foods are linked to enjoyment of life. Weight loss is stigmatized. To convince an obese person who feels like he/she is 'having the best of life' to change his/her lifestyle is an enormous challenge, especially if asked: 'What constitutes health?'"

ABSTRACT

Background: Between 2010 and 2030, a 69% increase in type-2 diabetes is expected in low-income countries compared to a 20% increase in high income countries. Yet health system responsiveness to non-communicable diseases has been slow in sub-Saharan Africa. Data on the prevalence of type 2 diabetes and its associated factors in mainly rural settings is lacking, yet such data can guide planning for diabetes control.
Objective: The aim of these studies was to assess the prevalence of type 2 diabetes, its risk factors, risk perceptions, and possible screening tools among people aged 35-60 years so as to inform primary care level intervention in rural low-income settings.
Methods: Four studies (I-IV) were conducted among people aged 35-60 years in a mainly rural demographic surveillance site in eastern Uganda (2011-2013). Study I, a cross-sectional survey assessed the prevalence of diabetes-related risk factors (including overweight, hypertension and seven socio-behavioural risk factors) in 1,656 people. Study II then estimated the prevalence of abnormal glucose regulation (AGR) using fasting plasma glucose (FPG), and assessed its socio-behavioural correlates in 1,497 people. To compare the utility of FPG and glycated haemoglobin (HbA$_{1C}$) rapid tests in risk stratification, a comparative survey of 795 people was nested into study II (Study III). To assess perceptions about diabetes, 12 Focus Group Discussions were conducted among people afflicted or at higher risk of type 2 diabetes (Study IV). The assessments used standard measurements and cut-offs.
Results: About 18% of people aged 35-60 years were overweight, while 21% had hypertension. Women (OR 3.7; 95% CI 2.7-5.1), peri-urban dwellers (OR 2.5; 95% CI 1.5-3.0), and wealthier people (OR 4.1; 95% CI 2.4-7.0) were more likely to be overweight. Only 34% had adequate knowledge about lifestyle diseases (I). Prevalence of diabetes was 7.4% while pre-diabetes was 8.6% and 20.2% with WHO and American Diabetes Association criteria respectively (II). Prevalence of AGR was twice higher in obese people compared to those with a normal BMI (APRR 1.9, 95% CI 1.3-2.8) (II). Sufficient physical activity and diverse diet were associated with lower likelihood of AGR (II). The direct medical cost of screening one person was US$0.53, translating to US$2 per person detected with AGR. Agreement between FPG (the reference) and HbA$_{1C}$ in classifying diabetes was moderate (Kappa=22.9; AUC =75%), while that for AGR was low (Kappa=11.0; AUC=59%) (III). However, agreement was high (over 90%) among negative tests and in participants with risk factors for type 2 diabetes. FPG was more practical than HbA$_{1C}$ (III). Participants' strong perceptions of diabetes as a very severe disease were incongruent with their perceived urgency for lifestyle change (IV).While people with diabetes perceive obesity as 'sickness', those without diabetes say it signifies 'success' (IV). Poverty, access to food and large families were cited as barriers to healthy diets. Domestic work was the preferred platform for physical activity increments.
Conclusions: Obesity, insufficient physical activity and unhealthy diets are possible aids to identifying people at higher risk of type 2 diabetes in primary care. Mass screening for abnormal glucose regulation may not be affordable to struggling health systems. However, rapid tests have utility in further evaluation of people with risk factors. Health education about lifestyle diseases is a priority and should target to change the community's notion of health and healthy lifestyles. Several challenges of adding NCD services to overstretched health systems come to light.

Key words: Type 2 diabetes, pre-diabetes, hypertension, abnormal glucose regulation, NCD prevention, low income setting, lifestyle, screening, primary care

LIST OF PUBLICATIONS

I.   **Mayega RW**, Makumbi F, Rutebemberwa E, Peterson S, Östenson C-G, Tomson G, Guwatudde D (2012): Modifiable Socio-Behavioural Factors Associated with Overweight and Hypertension among Persons Aged 35 to 60 Years in Eastern Uganda. PLoS ONE 7(10): e47632. Epub 2012 Oct 15. http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0047632

II.   **Mayega RW**, Guwatudde D, Makumbi F, Nakwagala FN, Peterson S, Tomson G, Östenson C-G (2013): Diabetes and Pre-Diabetes among Persons Aged 35 to 60 Years in Eastern Uganda: Prevalence and Associated Factors. PLoS ONE 8(8): e72554. Epub 2013 Aug 14. http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0072554

III.   **Mayega RW**, Guwatudde D, Makumbi F, Nakwagala FN, Peterson S, Tomson G, Östenson C-G (2014): Comparison of fasting plasma glucose and haemoglobin A1c point-of-care tests in screening for diabetes and abnormal glucose regulation in a rural low income setting. Diabetes Research and Clinical Practice pii: S0168-8227(13)00464-6. doi: 10.1016/j.diabres.2013.12.030. [Epub ahead of print]: http://www.diabetesresearchclinicalpractice.com/article/S0168-8227%2813%2900464-6/fulltext

IV.   **Mayega RW**, Etajak S, Rutebemberwa E, Tomson G, Kiguli J: 'Change means sacrificing a good life': Perceptions about severity of type 2 diabetes and preventive lifestyles among people afflicted or at high risk of type 2 diabetes in Iganga Uganda (Submitted)

These papers will be referred to by their Roman numerals I – IV

CONTENTS

LIST OF ABBREVIATIONS

ADA	American Diabetes Association
AFRO	Africa Regional Office (World Health Organisation)
AGR	Abnormal Glucose Regulation
AOR	Adjusted Odds Ratio
APRR	Adjusted Prevalence Rate Ratio
AUC	Area Under the Curve
BMI	Body Mass Index
BP	Blood Pressure
CHW	Community Health Worker
CI	Confidence Interval
COR	Crude Odds Ratio
CV	Coefficient of Variation
CVD	Cardio-Vascular Disease
DSS	Demographic Surveillance Site
FDPS	Finish Diabetes Prevention Study
FGD	Focus Group Discussion
FPG	Fasting Plasma Glucose
HbA_{1C}	Glycated Haemoglobin
HC	Health Centre
HCII, III, IV	Health Centre – Level II, Level III and Level IV
HCW	Health Care Worker
HDSS	Health and Demographic Surveillance Site
HIC	High Income County
HIV	Human Immuno-deficiency Virus
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
LIC	Low Income Country
LMIC	Low- and Middle-Income Country
MOH	Ministry of Health, Uganda
NCD	Non-communicable Disease
OGTT	Oral Glucose Tolerance Test
PHC	Primary Health Care
POC	Point-of-Care
PRR	Prevalence Rate Ratio
ROC	Receiver Operating Characteristic
SES	Socio-economic status
SIDA	Swedish International Development Cooperation Agency
SPSS	Statistical Package for Social Scientists
SSA	Sub-Saharan Africa
UBOS	Uganda Bureau of Statistics
UKDPS	United Kingdom Diabetes Prevention Study
UN	United Nations
UNMHCP	Uganda National Minimum Health Care Package
US$	United States Dollar
WHO	World Health Organisation
QALY	Quality Adjusted Life Year

OPERATIONAL DEFINITIONS

Abnormal glucose regulation: An abnormality in the body's metabolism of glucose, manifested as above-average levels of blood sugar or its associated parameters. It is a continuum that includes diabetes and pre-diabetes states (WHO and IDF 2006)

Health system: That complex whole that includes the organisation of people, institutions and resources to deliver health care services to meet the health needs of target populations (WHO 2007)

Higher risk person for type 2 diabetes: In this thesis, defined as a person with one or more risk factors for type 2 diabetes

Lifestyle: It is the typical way of life of an individual, group or community. It is shaped by individual choices and external (societal and environmental) influences (Stuckler and Siegel 2011)

Modifiable risk factors: Risk factors for a disease that can be altered by making appropriate interventions of a pharmacologic, behavioural, psychosocial or environmental nature (Lagerros and Rossner 2013)

Most-at-risk person for type 2 diabetes: In this thesis, defined as a person with abnormal glucose regulation. Abnormal glucose regulation has been shown to represent the highest risk status for development of type 2 diabetes (Chen et al. 2003)

Non communicable disease: A disease condition that is not directly transmitted from one person to another (WHO 2011c)

Prevention: Actions taken before the occurrence of a disease in an individual or a community to minimize the possibility of its occurrence. It includes primary prevention (at the community level) and secondary prevention (at the health facilities)

Risk stratification: The process of categorizing people on the basis of their level of risk for a particular health condition, using physical, biological or psychosocial parameters (Mendis et al. 2007)

Screening: A strategy for identifying people with unrecognized disease or high risk states. It can be based on laboratory tests or by checking for symptoms closely associated with the disease. Screening is 'targeted' when it is selectively done for a particular category of people (Gordis 2008)

Self-monitoring of health: Refers to actions taken to monitor one's own health. They may include periodic checks on physical, physiological and psychosocial parameters as well as the adherence to drugs and lifestyle adjustments

PREFACE

That mid-morning telephone call was no ordinary one. Maternal instinct told her, well before the caller's pronouncement, that the situation was irredeemably hopeless. She did not hide any emotion when she cried out, arms stretched in a resigned stance: 'My son is dead! Parents are not supposed to bury their children - it should be the other way round'. Shortly after saying that, she, a known hypertensive, fainted.

The young man in question had only been outwardly ill for less than four weeks. Even then, the illness did not appear that serious to the handful of people he had confided in. Only recently had he complained of feeling 'weak'. He had continued to report for work every day despite feeling unwell – urgent deadlines had to be met. The only health workers he had consulted when in control of his life were at a local private clinic. He was first treated for malaria. It was during one of the consultations that he had challenged the health workers, using his lay knowledge of medicine: 'why don't you check my urine sugar?' They discovered he had ketones in his urine. A diagnosis of type 2 diabetes ensued, and he was started on two classes of oral medications to control his blood sugar. (Three weeks later…) Following a set of distress calls that fateful morning, his second line of confidants had come to the same conclusion – that he had to be rushed to the referral hospital. He had fainted and slipped into a comma while explaining something on the phone! The hospital team was fast, but his blood pressure could not hold up and his sighing breaths worsened. He passed away, quietly, after approximately three hours of rigorous resuscitation. The autopsy raised eyebrows – he had suffered a massive but silent myocardial infarction (a heart attack), exacerbated by his metabolic condition.

As a witness to this hullaballoo, several questions popped up in my mind. How could such a thing have happened to a person only in his third decade of life? He had just bought a new car, baptised his daughter (one of two little children), and was roofing his new house. For an illness that often progresses slowly, how could it have evaded the radar to this tragic point? Truth be told, some premonitions came months ago. He had gained an awful load of weight and, according to confidants, even had a hypertension scare. What should it have taken for him to act in time to disarm the hands of death? The lurking answer to each question was the need for action.

Millions of people are trapped in a lifestyle of risk. A seductive environment plays on the psyche to curtail healthy choices. The semblance of enjoyment that a world of sedentariness, obesity, carbohydrate cravings and fried food brings has compromised human resilience in a species known to survive by adapting. Trim college graduates change rapidly after studies. A white-collar job and a car mean they sit more. Disposable income attracts previously inaccessible amenities. Subliminal dietary indulgence takes over. The same vagaries have permeated the rural folk, entrapping them too in a culture of pervasive repose. Traditional foods rich in fibre and minerals are disappearing from the dinner table, replaced by cheap refined foods. The villager, known to be a work-horse, has increasingly retreated to a passive keeper. For one third of the last decade, I have tried to study type 2 diabetes. However, the avoidable death of that man catalysed my resolve to act. This thesis, my humble contribution to a thirsty knowledge space, highlights some options for strengthening diabetes care and prevention in a low income setting. For while death is inevitable, lifestyle related deaths among thirty-something-year-olds are highly preventable.

1 BACKGROUND

1.1 RISING BURDEN OF NCDs IN LOW INCOME COUNTRIES

Non-communicable diseases (NCDs) have become a leading global health challenge. Taken together, NCDs represent the single largest cause of mortality in adults worldwide. Of an estimated 57 million deaths that occurred globally in 2008, 36 million (i.e. 63%) were due to NCDs (WHO 2011c). The leading causes of NCD-attributable mortality are cardiovascular diseases (CVDs), cancers, chronic respiratory diseases and type 2 diabetes. As the populations of more countries age, these numbers will rise. Although the NCD burden is highest in the higher income countries (HICs) (WHO 2011b, WHO 2011c), emerging evidence shows that future rise in NCDs will be disproportionately higher in low- and middle-income countries (LMICs) compared to the HICs. Already, nearly 80% of deaths due to cardio-vascular diseases occur in low- and middle-income countries (Cooper et al. 1998, Seedat 2007). Estimates from 23 high burden low- and middle-income countries show that NCDs were responsible for 64% of all deaths (Alwan et al. 2010).

Because mortality is a natural consequence of aging, premature mortality is a better indicator of the impact of NCDs on a population than crude mortality. In low- and middle-income countries, NCDs are increasingly occurring in younger working age people compared to the higher income countries (Unwin and Alberti 2006), affecting the economic wellbeing of their dependants. About 30% of NCD related deaths in LMICs occur in people aged less than 60 years, compared to 13% in the HICs (WHO 2011c). In 2008, NCD attributed age-standardised death rates were estimated to be 65% higher in low-income compared to higher income countries (WHO 2011c). NCDs are the leading causes of death in all regions of the world except for Africa. However, while NCD deaths are projected to increase by 15% globally between 2010 and 2020 the greatest increases will be in Africa and South-East Asia, where they will increase by over 20%. In contrast, there will be no significant rise in NCDs in Europe (WHO 2011c). NCDs are projected to cause almost three-quarters as many deaths as communicable, maternal, perinatal, and nutritional diseases combined by 2020, and to exceed them by 2030 (WHO 2011c). Indeed in some sub-Saharan Africa countries such as Mauritius and Seychelles, NCDs are already the leading cause of mortality, responsible for 40% of all deaths (Bovet et al. 2007).

The increase in NCDs is attributed to interrelated changes in population-level demographic, social and economic factors influenced by globalization (de-Graft Aikins et al. 2010, Maher et al. 2010). This state is often referred to as the 'Epidemiological Transition' (Omran 1971). Propelling the upsurge of NCDs is the growing prevalence of their associated risk factors, especially hypertension, smoking, harmful alcohol taking, insufficient physical activity and obesity/raised cholesterol. Obesity is fuelled by increasingly sedentary lifestyles short on physical exertion and high on risky foods (sugar, saturated fats, and refined carbohydrates) (Addo et al. 2007, Hossain et al. 2007) in a growing culture of chronic over-nutrition. In LMICs such risk factors are concentrated in a burgeoning middle class in the urban areas. However, available evidence though patchy, shows that these risk factors are increasing in the rural areas due to rapid adoption of 'western' lifestyles and increasing access to unhealthy food.

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Proven cost-effective strategies are available for reducing chronic disease risk, including both population-wide and individual risk approaches (Lim et al. 2007, Mendis et al. 2007, Simmons et al. 2010). Several studies have demonstrated that behavioural interventions substantially lower the risk of diabetes in people with Impaired Glucose Tolerance (IGT) (Pan et al. 1997 , Knowler et al. 2002). The Finnish Diabetes Prevention Study (FDPS) (Lindstrom et al. 2003) and its replica studies using the 'FINDRISK' tool in the Americas and Asia consistently show that intensive interventions targeted to high risk persons can sustainably reduce incidence of type 2 diabetes. Other evidence shows that community level pragmatic interventions too can substantially reduce cardio-vascular risk factors. Learning from the controlled trials, Finland initiated a massive country wide prevention program for NCDs, and there is evidence of pay-offs in reducing some risk factors at the national level (Rautio et al. 2014). The Västerbotten and Norsjo community studies in Sweden and the Otsego-Schohaire county study in New York state also provide examples (Weinehall et al. 2001a, Weinehall et al. 2001b). However, while evidence of efficacious interventions has been widely demonstrated in high income countries, very little of such evidence has been generated from sub-Saharan Africa (Bischoff et al. 2009). Results of one of the few such pilots in Cameroon indicate that appropriate NCD programmes can be achieved in sub-Saharan Africa by optimizing human resources and the health system (Bischoff et al. 2009).

The NCD agenda is gaining momentum globally. In May 2004, the 57th World Health Assembly adopted a major resolution on NCDs that calls upon WHO member states to develop strategies to address this growing problem. The same assembly adopted the WHO Strategy on Diet and Physical Activity. On May 13, 2010, the United Nations General Assembly (UNGASS) passed resolution 265 on 'Prevention and control of non-communicable diseases', a major political statement calling on Heads-of-State to address NCDs. In September 2011, the UN General Assembly convened a 'High Level' plenary meeting for Heads-of-State on NCDs. Out of this meeting, and its associated 'outcome document', is expected to come a series of programmatic steps by all UN members to address this growing global challenge (Alleyne et al. 2010). However, progress may not be as fast as the urgency for action merits.

Rising burden amid data scarcity: The rising burden of NCDs in low income countries is not matched by availability of context specific data, yet such data are crucial for planning and monitoring. NCD surveillance systems in most LICs are weak (WHO 2011c). Available data is patchy, very localized, and variable both in quality and methods. NCD data are often not sufficiently integrated into national health information systems (WHO 2011c) while health facility records are grossly incomplete due to under-diagnosis.

Due to the glaring gaps in routine data, epidemiologic studies provide the bulk of the current evidence for understanding NCDs in sub-Saharan Africa. Three key publications provide a synopsis of the burden of NCDs in Africa: 1) The article 'NCDs in SSA: What we know now' (Dalal et al. 2011) is a systematic review of epidemiological studies in the region. It shows that prevalence of NCDs varies considerably between countries, urban-rural gradients and some sub-populations. However, community based epidemiological studies are few and among these, South Africa and urban areas are over-represented. By 2010, only nine African countries had conducted national NCD surveys (Hall et al. 2011). 2) The WHO Global status report on NCDs (WHO 2011c), and 3) the WHO Atlas of African Health Statistics

2011 (WHO-AFRO 2011), present estimates from epidemiological studies and show that SSA has a substantial burden of NCDs.

However the modelling of NCD burden for sub-Saharan Africa in these global reports is based on critically few studies some with inadequate sample sizes, low representation of rural areas and infrequent repetitiveness (Hall et al. 2011). Key projections for Africa are therefore likely to be inaccurate because some assumptions carried from studies in HICs do not hold for sub-Saharan Africa - for example, while estimates in these global status reports show that obesity in HICs is higher in men, findings from most population-based studies in sub-Saharan Africa are contrary.

1.2   TYPE 2 DIABETES

Diabetes Mellitus is a health-threatening NCD with increasing prevalence worldwide. It is characterized by chronic hyperglycaemia, leading to micro-vascular complications affecting the kidneys, eyes and peripheral nerves and macro-vascular complications affecting blood vessels and the heart. According to Shaw et al, the world prevalence of diabetes among adults was estimated at 6.4% in 2010. Current projections by the International Diabetes Federation's (IDF) 6th Edition of the World Diabetes Atlas show that there were 382 million people with diabetes in 2013 and the number is expected to rise to 599 million (or 8% prevalence) by 2035 (IDF 2013).

Table 1: Trends in world-wide prevalence of diabetes and projected prevalence by 2035

2000	177 Million	Global Burden of Disease Study WHO
2003	194 Million	IDF Atlas 2nd Edition
2010	285 Million	Shaw et al 2010
2030	522 Million	IDF Atlas 5th Edition
2035	592 Million	IDF Atlas 6th Edition

The prevalence of type-2 diabetes is rising in sub-Saharan Africa too (Mbanya et al. 2010, Maher and Sekajugo 2011). According to the World Diabetes Foundation, there were an estimated 7.1 million cases of diabetes in Africa in 2003. Diabetes accounted for an estimated 6% of deaths in Africa in 2010 (Roglic and Unwin 2010). Between 2010 and 2030, a 69% increase in type-2 diabetes is expected in low-income countries compared to a 20% increase in high income countries (Shaw et al. 2010). This increase will result in substantial strain on health systems already facing a high burden of communicable diseases (Abegunde et al. 2007, Mbanya et al. 2010).

Some types of diabetes arise at younger ages in Africa, with socio-economic consequences to affected families. The rate of undiagnosed diabetes in sub-Saharan Africa is high (Mbanya et al. 2010). Individuals who are unaware that they have diabetes are at very high risk of chronic irreversible complications. A summary of the prevalence of type 2 diabetes in sub-Saharan Africa is provided in three recent publications: 1) Diabetes in SSA 1999-2011 (Hall et al. 2011), which is a systematic review; 2) New insights on diabetes mellitus and obesity in Africa part 1 (Kengne et al. 2013a), also a systematic review, and 3) the IDF Atlas 6th Edition (IDF 2013).

According to Hall et al, type 2 diabetes accounts for over 90% of diabetes cases in SSA. Diabetes prevalence varies between countries and rural-urban gradients, from 0.6% in rural Uganda to 12% in urban Kenya (Hall et al. 2011). Reported type 1 diabetes prevalence is low (from 4 per 100,000 in Mozambique to 12 per 100,000 in

Zambia). Gestational diabetes ranged from 0% in Tanzania to 9% in Ethiopia. 40% of people with diabetes were not aware of their condition (Hall et al. 2011).

There is insufficient data on the prevalence of diabetes in rural settings in SSA. Available surveys are patchy, with many countries and rural contexts under-represented (Kengne et al. 2013a). Most of the available studies took a whole population view (Mbanya and Ramiaya 2006, Mbanya et al. 2010, Oladapo et al. 2010, Dalal et al. 2011, Hall et al. 2011, Maher et al. 2011), few focusing on higher risk age-groups. Population-wide studies tend to return very low levels of prevalence especially in the rural areas because they include younger participants at much lower risk. More prevalence studies that target most-at-risk sub-groups are needed (like people older than 30 years) to generate evidence for targeted interventions.

Type 2 diabetes in Uganda: Uganda has a predominantly agrarian economy with increasing urbanization and a rapidly growing population. While communicable diseases and acute maternal/perinatal conditions comprise about 70% of the burden of disease (MOH 2010a), the burden of NCDs is increasing too. The most common NCDs in Uganda are: diabetes, hypertension and cardiovascular diseases, and some cancers. In the 1960s, diabetes was rare in Ugandan. However, three decades later the National Referral Hospital registered over 5,000 new patients in a five year period in the 1990s, according to un-published reports from the Ministry of Health (Sensasi 2006). Similar trends have been registered in up-country hospitals. In Mbale regional referral hospital (Eastern Uganda) diabetes cases increased from 80 patients per year in 1994 to over 600 per year in 2004, from the same unpublished reports. A 10-fold increase in type 2 diabetes is projected between 2005 and 2025 (Sensasi 2006). The highest occurrence is recorded in the Central Region (Sensasi 2006), probably due to higher socio-economic status, urbanisation, and adoption of western life-styles.

An unpublished report by the Ministry of Health entitled 'A rapid assessment of morbidity and mortality due to NCDs in Uganda' shows that diabetes accounts for 25% of NCD related deaths among people hospitalized due to NCDs. This report estimated that there were 74,354 newly diagnosed diabetes cases in health facilities in the financial year 2009/10 compared to 58,523 in 2005/06 representing a 27% increase over five years. Maher and colleagues estimate that there are about 98,000 diagnosed people with diabetes in Uganda, with an expected increase to 328,000 by 2030 (Maher et al. 2010). These estimates are way below those of the Uganda Diabetes Association which indicates that about 4% of Ugandans (or 1,120,000 people) suffer from type 2 diabetes. Uganda's public health system is therefore only handling a fraction of the burden of diabetes in the country. The rest are likely to die un-detected in the community, or to seek remedies from alternative practitioners.

There have been very few population-based studies on the prevalence of type 2 diabetes in Uganda. A cross-sectional study in Kampala and Mukono Districts in 2002 estimated the prevalence of type 2 diabetes to be 8% among people aged ≥35 years (Lasky et al. 2002). However, these districts have a mainly semi-urban population. Another survey in rural southern Uganda estimated the prevalence of diabetes at 0.6% (Maher et al. 2011). That survey however did not provide age-specific prevalence rates yet it included a wide age range (≥13 years).

As a key knowledge gap, estimates of the burden of diabetes in Uganda are patchy. More surveys with a rural and higher risk focus are needed to estimate the number of most-at-risk persons that need care. Without specific evidence from prevalence data,

it is difficult to justify where to target scarce resources (Lindstrom and Tuomilehto 2003, Ambady and Chamukuttan 2008).

1.3   RISK FACTORS FOR TYPE 2 DIABETES

Decades of research have shown that much of the burden of chronic diseases is attributable to multiple lifestyle factors working collectively. Proximate risk factors for type 2 diabetes are obesity, family history, insufficient physical activity, raised cholesterol, tobacco use, harmful use of alcohol, unhealthy diets and hypertension. Studies have also shown a link between NCDs and stress (Eriksson et al. 2008, Eriksson et al. 2013). Lindenberg, Ostergren and colleagues have cited a close association between psychosocial stress and exhaustion with disease (Lindeberg et al. 2011). Because all these factors are modifiable, NCDs are to an extent preventable (Miranda et al. 2008). Personal lifestyle measures to reduce risk of type 2 diabetes have been known for decades (Stuckler and Siegel 2011, Lagerros and Rossner 2013, Schellenberg et al. 2013). They include: Healthy diets, physical activity and regular monitoring of health parameters (body weight, blood sugar, blood pressure, blood lipids, and adherence to therapy) (Pan et al. 1997 , Booth et al. 2013). Others are cessation of smoking and harmful alcohol intake (Stuckler and Siegel 2011).

While sedentariness is highest in HICs, high levels are now increasingly seen in some LMICs (WHO 2011c). Smoking is still low in many LICs but data from 23 high burden LMICs shows that it is increasing (Alwan et al. 2010). Adult per capita consumption of alcohol is highest in HICs, but nearly as high in some LMICs, especially of local potent brew (WHO 2011c). Dangerous alcohol consumption has also been linked to other lifestyle diseases (Choudhry et al. 2014). Unhealthy diets are rising in lower-resource settings. In some countries in sub-Saharan Africa (e.g. Ghana, South Africa and Cameroon), hypertension has increased to epidemic proportions (Fezeu et al. 2006, Thorogood et al. 2007, Bosu 2010). Overweight has tripled in sub-Saharan Africa over the last two decades (Hossain et al. 2007).

A synopsis of the distribution of risk factors for type 2 diabetes in sub-Saharan Africa is presented in three systematic reviews: (Addo et al. 2007, Dalal et al. 2011, Kengne et al. 2013a). According to these reviews, prevalence of risk factors varies considerably between countries, urban-rural gradients and gender. Obesity rates ranged from 0.4 to 43%; smoking from 0.4% to 71%. Hypertension is the most frequently reported cardiovascular risk factor in Africa, with prevalence ranging from 4% to 65% across contexts (Dalal et al. 2011, Kengne et al. 2013a). Hypertension is consistently equal in men and women, higher in urban areas, and increases with age (Dalal et al. 2011). Less than 40% of people with hypertension have been detected and of those detected, less than 30% are on treatment. For those on treatment, less than 20% are controlled (Dalal et al. 2011).

Most evidence on cross-linkages between risk factors for type 2 diabetes is from high income countries (Mendis et al. 2004) and may not apply to other contexts (Miranda et al. 2008). For example, contrary to what is observed in Europe, obesity in Africa is predominant among women compared to men, but smoking is higher in men (Dalal et al. 2011). More than half of the LMICs are in the early stage of the nutritional transition (Abrahams et al. 2011). The distribution of overweight in such countries is still socially segregated, wealthier persons being more likely to be obese (Fezeu et al. 2006, Subramanian et al. 2009). Some data however show that in transitioning countries, obesity is increasingly occurring in low socio-economic status groups

(Hossain et al. 2007). Some transitioning countries face the paradox of families in which the children are underweight and the adults are overweight (Hossain et al. 2007).

The 'degenerative' models of NCD causation pay little attention to processes that build up to the optimal phenotypic state leading to disease (Miranda et al. 2008). Known 'proximate' risk factors are in reality underlied or modified by other context specific factors, yet few studies explore these relationships. Effective prevention requires unravelling these root causes of risk (Miranda et al. 2008). These underlying causes are often deeply rooted in a society and, in complex causal pathways, act across an individual's life course, driven by societal norms (Penn et al. 2013), to create the optimal phenotypic state for type 2 diabetes ('developmental hypotheses') (Miranda et al. 2008). Quoting the book 'Sick Societies', 'societies in which people are born, live, and age create the individual's risks for chronic diseases, for which individuals have little choice'(Stuckler and Siegel 2011).

Studies on the distribution of type 2 diabetes related risk factors in sub-Saharan Africa are patchy, with many contexts especially the rural areas insufficiently explored (Dalal et al. 2011). Even fewer studies have assessed the cross linkages between risk factors (WHO 2011c) yet latent factors are important in contextualizing interventions. Three population-based studies on the prevalence of CVD risk factors in Uganda and another in Cameroon focused on demographic correlates of either hypertension or abnormal glucose regulation (Lasky et al. 2002, Fezeu et al. 2006, Wamala et al. 2009, Maher et al. 2011) but did not include behavioural correlates. The lack of a holistic assessment of socio-behavioural risk factors is noticeable in other studies in sub-Saharan Africa (Addo et al. 2007, Mbanya et al. 2010, Dalal et al. 2011, Hall et al. 2011).

Likewise, very few studies have explored community perceptions about risk and preventive behaviours. Therefore, while the recommended behaviours are well known, there is inadequate information on forms of these behaviours that are feasible within the normative contexts of communities in sub-Saharan Africa (Whyte 2012). Lifestyle measures ought to be relevant to the context in which they are applied (Carmoi et al. 2008).

1.4   EARLY DETECTION, DIAGNOSIS AND MANAGEMENT OF DIABETES

Individual targeted interventions for prevention of type 2 diabetes require risk stratification and/or diagnosis (Beaglehole et al. 2008). People with type 2 diabetes often undergo a long pre-disease period during which they are exposed to detectable risk factors (Lindstrom et al. 2003, Ambady and Chamukuttan 2008). Many of these risk factors can be assessed in primary care, providing an opportunity for risk stratification. Concurrently, measurable metabolic changes occur, often referred to as 'the metabolic syndrome'. Pre-diabetes, the penultimate stage in these processes represents the 'most-at-risk' category for type 2 diabetes (Chen et al. 2003, Meigs et al. 2003, Edelman et al. 2004, Coronado-Malagon et al. 2009). Identifying individuals with pre-diabetes enables preventive measures to be invoked earlier (Anand et al. 2003, Waugh et al. 2007, WHO 2010b, Yoon et al. 2013). However, very few patients are detected early in LICs (Ambady and Chamukuttan 2008), losing an opportunity for prevention. Given the limited use of the Oral Glucose Tolerance Test (OGTT) in African surveys, the extent of undiagnosed diabetes and pre-diabetes is

less clear, but is probably high, in some contexts as high as 90% (Kengne et al. 2013b).

Risk stratification using biological markers requires valid, easy to use, affordable and acceptable tests usable at primary care facilities. Type 2 diabetes and pre-diabetes are detected either through an Oral Glucose Tolerance Test, Fasting Plasma Glucose (FPG) or Glycated Haemoglobin (HbA_{1C}). Diagnostic cut-offs for these tests have been defined by the WHO and the American Diabetes Association (ADA) (WHO and IDF 2006, ADA 2013). Pre-diabetes is defined by three criteria: Impaired Glucose Tolerance (determined by the OGTT), Impaired Fasting Glucose (determined by FPG) and HbA_{1C} levels between 5.7- 6.4%. However, due to resource constraints and late presentation, many health facilities in sub-Saharan Africa rely on random blood sugar (RBS) for diagnosis of diabetes. The debate about which tests are suitable for primary care screening in LICs continues. While the OGTT is the more sensitive test (Lyon et al. 2004), it has a lengthy cumbersome procedure, poor reproducibility, and questionable cost-effectiveness (Lyon et al. 2004, Wilson et al. 2009, Herman and Fajans 2010). FPG is easier, cheaper and more reproducible, but has lower sensitivity and high pre-analytical variability (Kumar et al. 2010).

In 2009, experts from the ADA, the European Association for the Study of Diabetes, and the International Diabetes Federation recommended that HbA_{1C} should be the primary test for early detection of type 2 diabetes and pre-diabetes in asymptomatic persons (ADA 2013). In 2011, WHO too recommended that HbA_{1C} is useful for diabetes screening, conditional to 'stringent quality assurance and standardization'(WHO 2011e). HbA_{1C} does not require fasting, and it is stable over 2–3 months (Jimeno Mollet et al. 2004, Kumar et al. 2010). However, it is costly (Herman and Fajans 2010) and it is affected by hemoglobinopathies, triglycerides, and common drugs like Aspirin (Kumar et al. 2010, Unnikrishnan and Mohan 2013). Evidence of its value in detection of pre-diabetes is also inconclusive (WHO 2011e).

Both the FPG and HbA_{1C} are now also available as point-of-care tests. However, their utility as PHC level screening tools for diabetes and abnormal glucose regulation is not yet clear, as is their feasibility for use by primary care workers.

Utility of risk scores: Because of the obvious financial constraints that PHC systems face in LICs, many countries cannot afford mass opportunistic screening for bio-markers. A worthy alternative to biomarker-based opportunistic screening is the use of risk scores (Beaglehole et al. 2008). Lindstrom and Tuomilehto demonstrated the utility of these 'risk engines' as simple, inexpensive, non-invasive and reliable tools to identify most-at-risk persons (Lindstrom and Tuomilehto 2003). Their model included age, body mass index (BMI), waist circumference, hypertension, physical activity, blood glucose, smoking, alcohol taking and diet as proximate predictors of diabetes risk. However, these factors include blood glucose measurement, which may not be affordable in low income settings. Another model called TAG-IT (Tool to Assess likelihood of fasting Glucose ImpairmenT) (Koopman et al. 2008) showed that age, sex, BMI, family history of diabetes, resting heart rate, and elevated blood pressure predict 74% of diabetes risk and BMI alone predicted up to 64% of risk.

Combinations of risk factors may therefore provide optimum prediction of risk for diabetes and could be the starting point for interventions. However, studies on such 'risk engines' have been mainly conducted in high income countries. Risk models relevant for Africa are lacking (Kengne et al. 2013a).

Care after diagnosis: Several studies from HICs (ACCORD, UKPDS, ADVANCE and VADT trials) show that treat-to-target interventions among diabetes patients can substantially slow the progression of micro-vascular damage, and therefore reduce the severe major complications like kidney disease, diabetic foot and retinopathy (Macisaac and Jerums 2011). However, evidence on overrall reduction of CVD related mortality remains equivocal, with some large trials like ACCORD showing that intensive interventions impact on CVD risk while others like the UKPDS show that they are not efficacious in this dimension (Macisaac and Jerums 2011). Intense interventions have also been associated with higher incidence of hypoglycaemia (Macisaac and Jerums 2011).

The substantial advances in treatment and care for type 2 diabetes seen in HICs are out of reach for many countries in sub-Saharan Africa where care for diabetes remains suboptimal (Kengne et al. 2013a). Because of this, there are low levels of glucose control among diagnosed cases (Hall et al. 2011). The majority of patients have irreversible complications at diagnosis, which impacts on treatment success, quality of life and cost of treatment. In the systematic review by Hall et al, the proportions of patients with diabetes related complications in different countries in sub-Saharan Africa ranged from 7-63% for retinopathy, 27-66% for neuropathy, and 10-83% for micro-albuminuria (Hall et al. 2011). Because patients present late, most of them require insulin as first line treatment. Novel and more stable insulins and drugs are not affordable for many countries. Five-year mortality of patients ranged from 4 to 57% (Hall et al. 2011). Access to HbA_{1C} monitoring for diagnosed cases is low. The Diabcare Africa study found that only 47% of patients in leading diabetes centres had at least one HbA_{1C} measurement over 12 months, ranging from 28% in Eastern Africa to 81% in some Central African countries (Kengne et al. 2013a).

According to the chronic care model (Bodenheimer et al. 2002), management of diabetes is increasingly a dynamic partnership between the patient and the service provider, the former having substantial autonomy in self-care. However, patients in Africa lack the amenities to take charge of their care (Kengne et al. 2013a). One study from Nigeria showed that only 27% of patients had access to home-based glucose monitoring devices (Kengne et al. 2013a). Attainment of lifestyle targets is sub-optimal in many settings while hypoglycaemia from treatment poses a higher threat than hyperglycaemia (Kengne et al. 2013a). Low access to refrigerators in rural areas means too that insulin is stored inappropriately. Patients have to travel frequently to health facilities for insulin refills because they cannot take longer term doses.

1.5   BEHAVIOUR CHANGE EDUCATION ON DIABETES IN LICs

Among proposed 'best-buys' at the population-level (priority actions to scale up the NCD response by countries), the WHO cites mass health education as a requisite strategy (WHO 2011c). The diffusion of health information on diabetes and NCDs in sub-Saharan Africa is low because in many settings the focus is on acute infectious diseases (Remais et al. 2013). Behaviour change theory indicates that awareness per-se may not necessarily change human behaviour but rather, adoption of health behaviours is a sequential process with different stages (Glanz et al. 2008). However several systematic reviews failed to demonstrate that the efficacy of interventions using the trans-theoretical model is dependent on the sequenced way in which lifestyle interventions are introduced (Tuah et al. 2011, Mastellos et al. 2014).

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At the individual level, planned behaviour is influenced by subjective norms and the environment (Ajzen 2011). The success of lifestyle interventions depends on realistic goal setting and relevant options (Health Quality Ontario 2009 , Bray et al. 2013), yet current approaches to health education are often provider centred (Angermayr et al. 2010, Gilstrap et al. 2013, Schellenberg et al. 2013). Because individuals are influenced by societal norms (Penn et al. 2013), lifestyle education ought to be relevant to the normative context in which it is applied (Carmoi et al. 2008). While the recommended lifestyles behaviours are well known, there is inadequate information on forms of these behaviours that are feasible within the normative contexts of communities in sub-Saharan Africa (Whyte 2012). Studies are necessary to explore models for roll out of lifestyle interventions in Africa.

1.6   ECONOMIC BURDEN OF TYPE 2 DIABETES IN LICs

It has been argued that primary prevention (by fighting major risk factors like tobacco use, alcohol abuse, risky diets and low physical activity) is more cost-effective than improving secondary care in fighting the NCD epidemic (Probst-Hensch et al. 2011). For 23 selected LMICs which account for 80% of the total burden of NCDs, an estimated US$84 billion of economic production will be lost from heart disease, stroke, and diabetes between 2006 and 2015 if nothing is done. Achievement of a global goal for NCD control (i.e. a 2% yearly reduction in chronic disease death rates over the next 10 years) would avert 24 million deaths in these countries, saving an estimated US$8 billion (i.e. 10% of the projected loss) (Abegunde et al. 2007). According to Hall et al (Hall et al. 2011), the annual cost of diabetes in SSA is estimated at US$67 billion, or US$ 8,836 per patient. The health budgets of virtually all countries in the region cannot cope with such costs, yet many more patients remain undetected (Kengne et al. 2013b).

Accumulating evidence shows type 2 diabetes is an impoverishing illness in low income countries (Kengne et al. 2013b). The annualized direct medical costs of diabetes treatment across private and public clinics in Khartoum for example was estimated at US$175, equivalent to about 9% of the annual wage of a patient with diabetes in this setting (Elrayah-Eliadarous et al. 2010). This cost excludes indirect expenditures on transport and food. The cost to the patient for the treatment of severe diabetic foot ulcers is equivalent to about two years of average annual income in Tanzania, compared to one years' wages in the USA (Kengne et al. 2013b). Patients with NCDs in rural settings in India pay considerably more than patients with communicable diseases, often obliterating household income and forcing them to rely on informal intra-family cross-subsidisation (Binnendijk et al. 2012).

Very little of the evidence on cost-effective prevention strategies has been generated from Africa (Jones and Geneau 2012). Modelling studies suggest that implementing the most effective interventions to control diabetes is likely more costly for African countries than other regions of the world (Kengne et al. 2013b). There is inadequate information on the economic benefit of population level interventions like health education compared to individual interventions like screening and intensified lifestyle programs. In Uganda, no studies have been conducted to assess the direct and hidden costs of diabetes although anecdotal evidence shows that patients spend substantially on drugs (due to frequent stock outs), blood sugar testing, treatment of complications, transport to the few diabetes clinics and long waiting times.

1.7   DIABETES AND NCDS IN STRUGGLING HEALTH SYSTEMS

The increasing incidence of chronic diseases in countries in sub-Saharan Africa is a challenge to their health systems (Dalal et al. 2011). On one hand, acute conditions are still responsible for a larger share of the disease burden (WHO-AFRO 2011). Six conditions (maternal/peri-natal problems, malaria, acute respiratory infections, diarrhoeal diseases, HIV/AIDs and TB) account for about 54% of the burden of disease in Africa (WHO-AFRO 2011) and 60% of the disease burden in Uganda (MOH 2010a). Primary health care systems in this setting have for long been designed to address these conditions (Maher et al. 2010), yet they still face major challenges regarding access, quality, utilisation and efficiency of existing services (Rutebemberwa et al. 2009, Waiswa et al. 2010).

Because NCDs now account for at least 20% of the disease burden in sub-Saharan Africa (Lopez et al. 2006) they can no longer be ignored or seen as a distraction from control of infectious diseases (Miranda et al. 2008). A 'dual burden of disease' is imminent (Dalal et al. 2011) yet health systems in the region have not adjusted fast enough (Maher et al. 2010). Many countries in Africa do not have established prevention programs for NCDs (Kengne et al. 2013b) and where they exist, the programs are much smaller in scale compared to those targeting communicable diseases (Samb et al. 2010, Kengne et al. 2013b). Capacity for control of NCDs varies considerably across countries, but is mostly inadequate (Alwan et al. 2010, Kengne et al. 2013b). Integration of care for both communicable and non-communicable diseases is low, yet opportunities exist for such integration (Remais et al. 2013).

A major shift towards enhancement of NCD control in the health systems of low income countries is therefore necessary (Beaglehole et al. 2008, Maher et al. 2010). However, because LICs already face many challenges, integration of NCD services requires significant strengthening of their health systems (Beaglehole et al. 2008). NCDs interventions should not be introduced as vertical programs (Remais et al. 2013). The challenge is how to build health systems that can balance both acute and chronic conditions, with sufficient quality, access and outcomes without 'crashing'. The system for delivery of interventions for NCD prevention is almost as important as the interventions themselves (Beaglehole et al. 2008).

In a context where PHC level strategies for NCDs are limited, examination of the health system building blocks (WHO 2007) highlights several challenges that need to be overcome. Applying this model, Samb et al determined that the factors that limit countries' capacity to implement proven strategies for chronic diseases relate to the way in which health systems are designed and function (Samb et al. 2010). A synopsis of some of the challenges is presented as follows:

Human resources: Sub-Saharan Africa has the lowest ratio of health workers to service population (WHO-AFRO 2011) compared to other regions. Many critical services are provided by auxiliary health workers (Bischoff et al. 2009). Integration of NCD packages would mean more workload. Although nurses will need to play a leading role in NCD care (Awah et al. 2008, Beaglehole et al. 2008, Bischoff et al. 2009), task shifting to auxiliary health workers will be inevitable. More evidence is needed on NCD service delivery tasks that can be shifted to other actors in the health system.

Services organisation and delivery: Service delivery packages in LICs were primarily oriented to communicable diseases (Maher et al. 2010, Remais et al. 2013) along with guidelines and job-aids. To meet the challenge of NCDs, primary health care services will have to be strengthened substantially (Strong et al. 2006) to reach communities, high risk individuals, and people with disease. Innovative packages of known efficacious strategies ought to be delivered to these three audiences with sufficient quality and cross-linkages (Beaglehole et al. 2008). Selection of appropriate pharmacologic, lifestyle and psychosocial measures based on efficacy, cost and feasibility is necessary (Beaglehole et al. 2008). Integration of NCD services may however disrupt other services substantially (Remais et al. 2013). Translational studies are needed on how NCD services can be layered into existing and innovative platforms with minimal disruption. 'Community-led' service delivery models, piloted in countries like Bangladesh, should be explored in sub-Saharan Africa. More evidence is also needed in defining most-at-risk populations, and in tailoring different services to different levels of care. Strengthening public-private partnerships in NCD service delivery is necessary too, since the private sector is responsible for a large portion of health service delivery in Africa (Rutebemberwa et al. 2009).

Diagnostics: There are calls to simplify the diagnosis of type 2 diabetes (Mostafa et al. 2010). The availability of effective point-of-care (POC) tests in primary care is increasingly necessary (Little 2005). With the low access to laboratories at primary care levels in sub-Saharan Africa, innovative approaches to risk assessment and stratification also need to be developed. Risk factor based algorithms that are amenable to use at primary care levels ought to be explored, especially those that can easily be implemented by nurses and community health workers.

Medicines and therapeutics: In health systems that lack essential drugs at PHC levels, identification of more people with disease is likely to exacerbate existing shortages (Beaglehole et al. 2008). Questions on the ethics of screening without ability to treat arise. Significant preparation for the leap in demand for treatment must precede any efforts at screening. Essential drugs should be made accessible, and contextually relevant therapeutic regimens developed, both pharmaceutical and lifestyle based.

Health Information: At the centre of the health system are the communities, high risk persons, and people with disease together with their families. Effective NCD services should be able to rally these audiences in mutually enhancing ways. Currently, the bulk of health education messages in sub-Saharan Africa is oriented towards acute conditions and infectious diseases (Maher et al. 2010). Culturally-relevant interventions require a clear understanding of the priority risk factors in the communities, how communities perceive risk in context, and their readiness to take up lifestyle adjustments. Such quantitative and qualitative data are lacking for many contexts in sub-Saharan Africa (Kengne et al. 2013b).

Financing: Few countries in Africa have met the pledge to spend 15% of their national budgets on health as per the Abuja Declaration (WHO 2011a). NCD integration would no doubt exacerbate financing challenges. Transfer of costs to individuals and families would escalate the high out-of-pocket expenditures already incurred by households (WHO-AFRO 2011). Uganda's government for instance spends about US$6 per capita on health compared to US$24 in out-of-pocket expenditure per-capita (WHO 2009). Interventions deployable at minimal costs with acceptable access, equity and effectiveness need to be explored for sub-Saharan Africa. The private sector, which in many countries accounts for a substantial share of

health service delivery, could also play a key role in NCD financing (Ghatak et al. 2008). More evidence is needed too on the cost-effectiveness of different service packages in Africa.

Governance and policy: Raising the priority of NCDs is a political process (Geneau et al. 2010). Countries that are still in the early stages of the NCD transition are especially important because structural measures can avert an NCD epidemic (Abrahams et al. 2011). On a positive note, there are indications that chronic diseases and NCDs are increasingly receiving more attention in Africa (Kengne et al. 2013b). As of 2010, 89% of African countries had a dedicated unit or its equivalent within the national Ministry of Health responsible for NCDs and 61% had funding available for NCDs. However, only about 26% of the countries had an operational policy or programme for type 2 diabetes (Kengne et al. 2013b). Policy makers urgently need to develop policies on NCD prevention to support the service delivery environment (Lachat et al. 2013). There would be need for substantial leadership at all levels. Robinson and Hort propose a four step reform process: 1) building political commitment and addressing systems constraints, 2) developing public policies on prevention, 3) creating new service delivery models and, 4) ensuring equity in access (Robinson and Hort 2012).

Learning from HIV care and communicable disease programs: There is a potential to learn from the successes in integration and scale up of HIV care in the development of a chronic care model for low income countries (Janssens et al. 2007), especially regarding quality of care, task shifting, intersectoral collaboration and enhancing adherence to therapy (Agnarson et al. 2010, Boruett et al. 2013). Important successes too have been registered in reduction of malaria, TB, and child mortality (UN Inter-Agency Group 2013, WHO 2013). These programs have different funding streams, and were re-energized by major global policy and funding agenda. Lessons on how such global commitments were realised can be applied to the NCD agenda.

NCDs and the Health System in Uganda: Uganda implements a level-based health care system for public health services (MOH 2010a): The 'Health Centre II' (HCII) (at parish level) serves about 5000 people, is nurse-led and implements the 'minimum activity package' (treating common diseases, antenatal care, immunisation, referral and outreaches) with no in-patient services. The 'Health Centre III' (HC III) (at sub-county level) is an intermediate facility serving about 25,000 people, with additional services including deliveries, limited in-patient care, maternity, TB treatment, and public health inspection services. It is headed by an auxiliary clinician cadre called a 'Clinical Officer' and has a laboratory for basic tests (malaria, urinalysis, blood sugar, anaemia and tuberculosis). The 'HCIV' and 'district hospital' are referral units serving about 100,000 people in a zone called a Health Sub-district. They have medical officers and provide referral services. They are also responsible for providing technical support to lower facilities and to plan for service delivery in the zone. Alongside the public health services, the private sector plays a key role, accounting for over 40% of service delivery. It includes 'not-for-profit' providers with service packages akin to those in the public health system often subsidised by government, and 'for-profit' providers with mainly curative services. Alongside formal health care are community health workers (CHWs). Their responsibility is mobilizing communities for health programs, health education and peer support.

Uganda has established an NCD Program Office in the Ministry of Health. NCDs have featured in the last three national health sector strategic plans (MOH 2010a).

Policies and regulations on tobacco and alcohol control have been implemented. The NCD coordinating office has rallied different stakeholders to form an 'NCD forum' which meets regularly to harmonize strategies. A food and nutrition policy is also under development by the Ministry of Agriculture. The Uganda NCD Alliance, a not-for-profit agency uses targeted advocacy and outreach to promote NCD action.

However, akin to other LICs, Uganda's strategy for NCD prevention is evolving (MOH 2010a). At the time of this thesis, Uganda's only official guidelines for type 2 diabetes were published in 1998 (Masaba et al. 1998). These guidelines focus on symptomatic persons in secondary care settings, and less on prevention. The Ministry of Health and partners are developing a set of new guidelines and job aids to enhance NCD service delivery in primary care. The current structure and delivery of services for type 2 diabetes and NCDs in Uganda has many gaps and opportunities. While the 'Uganda National Minimum Health Care Package' (UNMHCP) mentions NCDs (MOH 2010a), preventive services at the different service delivery levels are patchy. A synopsis of the current service packages at different levels of care and how they relate to NCDs are presented in Table 2 below using type 2 diabetes as a tracer:

Table 2: Current service delivery packages: Where are the NCD services in Uganda's PHC facilities?

Level	Characteristics and current package	NCD services (*Type 2 diabetes as an example*)
Health facility based		
Health Centre I	Village level (~500 people); Community Health workers (Home visiting, peer education and mobilization of people to attend immunisation and other outreaches)	Almost no involvement in diabetes related lifestyle education and patient support
Health Centre II	Parish level (~5000pple); Nurse-led; provide 'Minimum Activity Package (Identify/treat common conditions (outpatient), prevention outreaches, referral of complicated cases)	Predominantly malaria, acute respiratory infections, diarrhoea, immunisation and family planning; largely no services on diabetes prevention
Health Centre III	Sub-county level (~25,000pple); 'Intermediate referral' package (Auxiliary clinical services; limited in-patient care, maternity/deliveries, lab for tuberculosis, malaria, urine, haemoglobin	Can do blood and urine sugar tests but it is mostly for emergency obstetric care. Comprehensive HIV care provided in some of them but largely no diabetes prevention services.
Health Centre IV/ Hospital	At county/district level (~100,000pple); provides a 'Comprehensive activity package': Clinician led, caesarean section, minor surgery, blood transfusion, planning and management support for the health service zone	Provide diagnosis, treatment, follow-up of diabetes; diagnosis is mainly based on classical symptoms and Random Blood Sugar; often have the only public diabetes clinic in the health service zone; largely no diabetes prevention services
Private-for-profit clinics	Offer clinical services for common illnesses focusing on secondary care; they fill critical gaps in curative care	Diagnosis, treatment, follow-up of diabetes
Non-health facility based		
Private-not-for profit	They are major stakeholders in community based service delivery; they fill critical gaps in primary health care especially community mobilisation	Limited involvement in NCD prevention
Other Sectors outside health	Other sector activities e.g. education, gender, labour and agriculture have minimal direct involvement	Food policy under development; limited inter-sectoral actions targeting NCDs
Folk	Ill-structured; first and last resort; highly accessible	Opportunistic services because of the gaps in existing formal services

Although there are many opportunities to integrate preventive services for type 2 diabetes and NCDs into primary care in Uganda, a key knowledge gap exists regarding which service packages and specific actions can be integrated into existing PHC services at different levels without severely disrupting other services, and within the available resources.

1.8   SUMMARY OF THE KEY KNOWLEDGE GAPS

The rising burden of NCDs in low income countries is not matched by availability of context-specific epidemiological data regarding most-at-risk population sub-groups. Because surveillance systems for NCDs are weak, epidemiological studies are currently the main source of evidence yet available data are patchy, with inadequate representation of rural areas.

Few studies have assessed the prevalence of diabetes and pre-diabetes in higher risk population categories and rural settings in sub-Saharan Africa. Most of the available studies take a whole population view and return very low levels of prevalence especially for rural areas. There is need for more studies to describe the epidemiology of type 2 diabetes in higher risk population groups like people older than 30 years.

Few studies have characterized and quantified socio-behavioural risk factors for type 2 diabetes in low income settings, and even fewer studies have explored the underlying drivers of the proximate risk factors in sub-Saharan Africa. Knowledge of such drivers would allow interventions to target the root causes of the proximate risk factors.

There is limited data on the utility and cost implications of available screening tests that can aid in identification of the most-at-risk persons at primary care levels in sub-Saharan Africa. There is also limited data on suitable socio-behavioural correlates of abnormal glucose regulation that can be used to develop risk scores to help in identification most-at-risk persons. These risk scores could provide an alternative to screening which is likely not affordable in most primary care contexts in LICs. Risk stratification allows scarce resources to be targeted to most-at-risk groups.

Few studies have assessed the context specific perceptions of type 2 diabetes related risk factors, community perceptions regarding preventive behaviours and forms of these behaviours that are relevant and acceptable to target communities in rural Africa. This information is necessary to guide development of contextually relevant lifestyle interventions.

Although there are many opportunities to integrate preventive services for type 2 diabetes into primary care, a knowledge gap exists regarding which specific actions can be integrated at different levels of service delivery without severely disrupting service delivery, and within available resources. While a number of studies have demonstrated the effective strategies for type 2 diabetes prevention, very little of this evidence is coming from Africa. Basic information like direct costs of simple preventive procedures is lacking. More exploratory studies are needed to identify services that can be integrated into primary care and the implications to the health system of such integration.

2 PROBLEM STATEMENT AND RATIONALE

2.1 STATEMENT OF THE PROBLEM

This thesis focuses on four information gaps regarding the burden of type-2 diabetes and potential interventions for prevention and early detection of the disease in low-income settings in sub-Saharan Africa.

There is insufficient data on the prevalence of risk factors for type 2 diabetes in predominantly rural communities in sub-Saharan Africa. Existing data are patchy, with several countries and rural contexts under-represented. In addition, data on the socio-behavioural correlates that underlie key proximate risk factors like overweight and hypertension are lacking. These underlying drivers of risk are important for enriching behaviour change education messages and for identifying the priority target groups for health education (I).

Data on the prevalence of type 2 diabetes and pre-diabetes in rural contexts in sub-Saharan Africa are lacking. The few available studies with a rural outlook take a general population perspective and do not provide sufficient information on its distribution and correlates in higher risk population sub-groups like people older than 30 years. Available studies therefore present a gap in clarifying which age-group should be prioritised for targeted interventions, the proportion of most-at-risk persons and the prevalence of undetected disease. Such information is necessary to justify preventive action at the individual and population level (II), but can also be triangulated with cost data to estimate the direct medical costs of screening for identification of most-at-risk persons (II).

There is also insufficient information on suitable aids to identification of most-at-risk persons for type 2 diabetes in sub-Saharan Africa. Identifying individuals with abnormal glucose regulation enables intensified preventive measures to be invoked earlier. The utility of available rapid screening tests (FPG and HbA_{1C}) in aiding risk stratification at primary care levels has not yet been adequately evaluated in Africa. (III). In addition, data on socio-behavioural correlates of abnormal glucose regulation which can aid risk stratification as an alternative to laboratory screening, are needed since screening is likely not affordable for many contexts in sub-Saharan Africa (II).

Lastly, few studies have explored the communities' perceptions about recommended preventive lifestyles in Africa. Therefore, there is inadequate information on forms of these behaviours that are feasible, acceptable and relevant to the normative contexts of communities in sub-Saharan Africa. Without context specific options for lifestyle adjustment, behaviour change education messages targeting communities and individuals in rural sub-Saharan Africa may be irrelevant to their target audiences, especially regarding the normative environment affecting behaviour (IV).

2.2 RATIONALE FOR THE STUDIES

The majority of low income countries (including in sub-Saharan Africa) hardly have any large preventive programs for type-2 diabetes. As a result, most individuals with the disease present late, when life-style measures can no longer avert disease. There is insufficient information on how low income countries can approach the process of integration of prevention measures for type-2 diabetes in their essential health care

package. There is a need for evidence to back the selection of priority interventions at the community level, the health facility level and among higher risk persons.

The relevance of population-level lifestyle interventions is in empowering communities with sufficient knowledge to be able to make informed choices. However, there is need for evidence on the most prevalent risk factors and their correlates, to guide development of such health education tools.

Without prevalence data, it is difficult to plan for NCD prevention. Assessing prevalence in higher risk sub-groups (like people older than 30 years) clarifies whether the proportion of most-at-risk persons and people with disease necessitates urgent action, and whether it is justified to target services to specific sub-groups. The direct medical costs of detecting one most-at-risk person may also be determined, which in part illuminates the affordability of screening.

In low income countries where prevalence of type 2 diabetes is still relatively low, risk stratification is necessary to identify the most-at-risk groups, so as to allow targeted intervention. However this requires the availability of simple, accessible, and cost effective diagnostic tests that can be deployed at point-of-care in primary care settings. There is need to explore the utility of available point-of-care tests in aiding risk stratification in low income countries. As an alternative to the screening tests, knowledge of the socio-behavioural correlates associated with type 2 diabetes provides background information on relevant variables to include in a risk score for behavioural risk assessment. Where laboratory diagnostics are lacking, such risk scores could be the plausible tool for risk assessment.

Because individuals are influenced by societal norms, lifestyle measures ought to be relevant to the context in which they are applied. As an important part of the health system, health educators should be guided on the forms of recommended lifestyles that are relevant to the community norms in their specific cultural settings. This requires a context based assessment of how communities interpret the recommended measures for prevention of type 2 diabetes and how they can operationalize them.

Figure 1 below summarises the key study questions for this thesis and how they relate to the community, people with undetected risk factors or disease, and people with detected risk factors or disease:
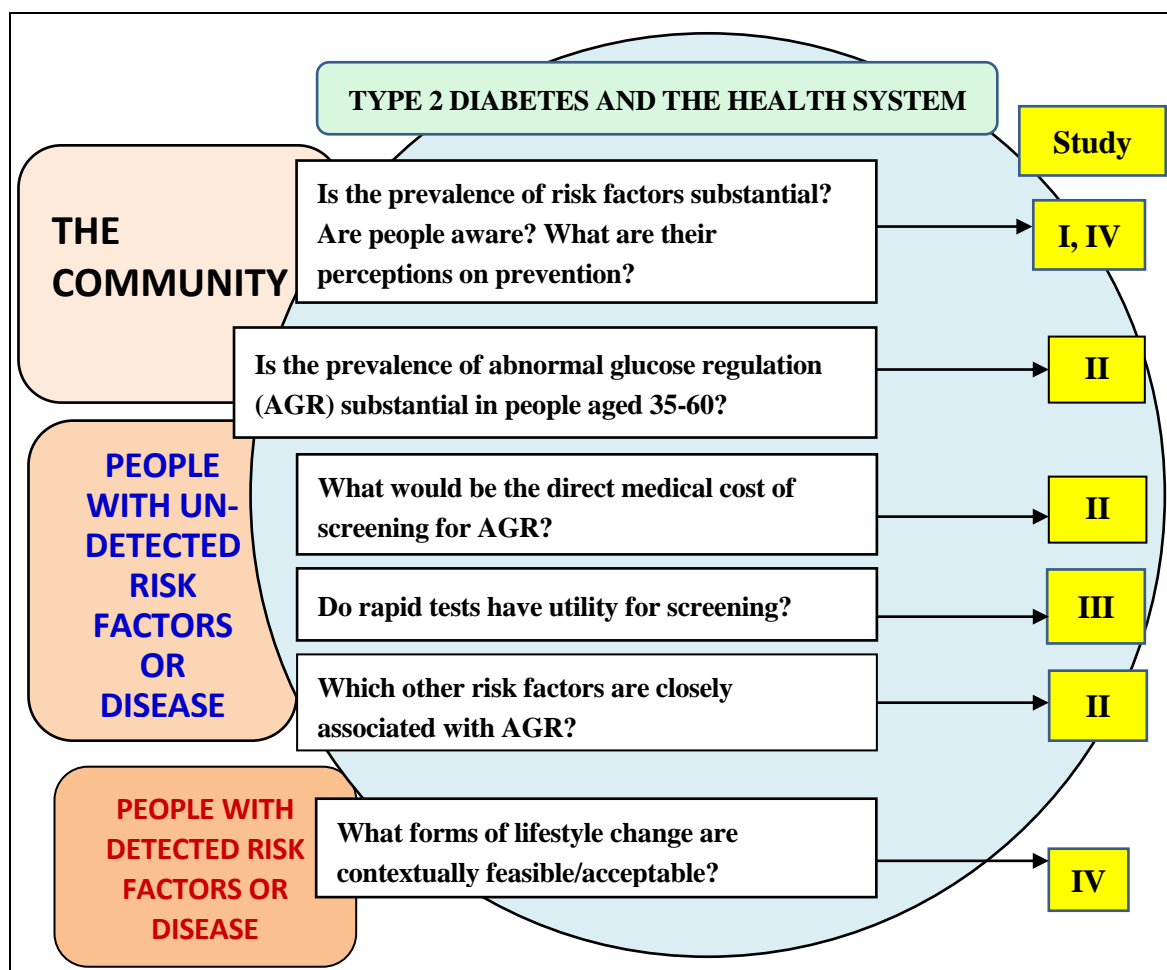
Figure 1: Conceptual framework: Type 2 diabetes - Prevalence, risk factors, perceptions and health system implications

At the centre of NCDs/type 2 diabetes services in the health systems of low income countries are three target audiences: The general community, people with undetected risk factors and disease (together with their families) and people with detected risk factor or disease (together with their families). At the community level, it is necessary to know the magnitude of type 2 diabetes related risk factors, whether people are aware about lifestyle diseases and their perceptions on prevention. It is also necessary to establish whether the prevalence of type 2 diabetes is substantial in people aged 35-60 years in the rural areas. For undetected risk and disease, knowledge of their magnitude clarifies the potential burden to the health system of their detection. The costs of screening can aid in computing the direct medical costs of such a screening program. It is also necessary to evaluate the utility of possible screening tests for use at primary care level. Knowing the socio-behavioural factors associated with AGR can inform the development of behavioural risk assessment tools. Among people with risk factors or disease, knowing their perceptions about prevention and the forms of lifestyle adjustments that are feasible to them can enhance lifestyle counselling by highlighting contextually relevant options. All this information can contribute to strengthening the health system responsiveness to type 2 diabetes prevention and care, in building an appropriate chronic care model for resource poor countries.

3 AIMS AND OBJECTIVES FOR THE STUDIES

3.1 GENERAL AIM

The aim of these studies was to assess the prevalence of type 2 diabetes, its risk factors, risk perceptions, and possible screening tools among people aged 35-60 years so as to inform primary care level prevention and management in rural low-income settings.

3.2 SPECIFIC OBJECTIVES

1. To determine the population level prevalence of type-2 diabetes related risk factors among people aged 35-60 years in a predominantly rural low income setting (Study I)
2. To estimate the population level prevalence of abnormal glucose regulation and its associated factors among people aged 35-60 years in a predominantly rural setting (Study II)
3. To compare the utility of two point-of-care tests in targeted screening to identify most-at-risk persons for type 2 diabetes in a predominantly rural low income setting (Study III)
4. To identify perceptions about severity of type 2 diabetes and preventive lifestyles among people afflicted or at higher risk of type 2 diabetes in a low income setting (Study IV)

4 METHODS

4.1 INTRODUCTION

This thesis is a compilation of four studies each providing descriptive findings on an aspect pertinent to prevention of type 2 diabetes at primary care levels in a low income setting. Study I assesses the prevalence of risk factors for type 2 diabetes at the population level among people aged 35-60. Study II then examines the prevalence of type 2 diabetes and abnormal glucose regulation (diabetes and pre-diabetes) in the same population. Study III explores the utility of two possible tests in population level screening for abnormal glucose regulation, a high risk state for type 2 diabetes. Study IV then explores perceptions about preventive lifestyles among people afflicted or with risk factors for type 2 diabetes.
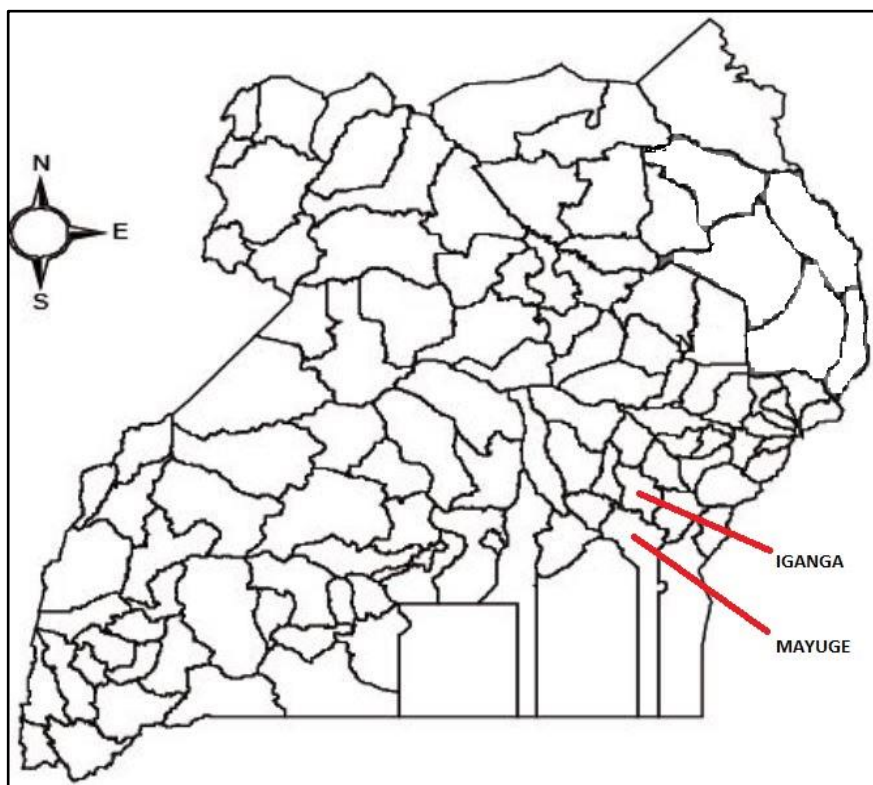
4.2 STUDY SETTING AND STUDY POPULATION

All studies were conducted in the Iganga-Mayuge Health and Demographic Surveillance Site (HDSS), located in two eastern Uganda districts of Iganga and Mayuge (Figure 2), approximately 120 kilometres from Kampala, the Capital of Uganda. Uganda is located in East Africa. Iganga and Mayuge are part of eight administrative districts of the Busoga region.

In 2012, Iganga District had an estimated population of 466,200 (Uganda Bureau of Statistics 2007). The district has 101 health units, 83 of which (82%) are government owned. There is one general hospital (which provides referral services and hosts the only diabetes clinic in the district), three HC IV and 27 HC III. The rest are HC II. Mayuge District had an estimated population of 461,200 in 2012 (Uganda Bureau of Statistics 2007). It has one private-not-for-profit hospital (patients pay some subsidised user fees), two HC IV (all government owned) and 35 HC II. Mayuge district contributed only 10% of the study participants due to the geographical spread of the HDSS.

Approximately 90% of the population in both districts resides in the rural areas while 7% are peri-urban. Small scale agriculture is the main economic activity, but petty trading is common in the semi-urban areas and fishing in the lake shore areas. The main language in the region is 'Lusoga' a Bantu dialect.

The HDSS is a geographical portion of these two districts, with a population of approximately 80,000 people in 65 villages. It has one town comprised of 13 villages (hereafter referred to as 'peri-urban areas'); the rest (80%) of the villages are rural. Apart from the routine demographic surveillance activities, add-on studies are often conducted within the HDSS, including this study. Data was collected in May-June 2011 (I), March-April 2012 (II, III), and April-May 2013 (IV). The study population comprised adult men and women aged 35-60 years within the HDSS. All studies have focused on this particular age-group because of its higher likelihood for type 2 diabetes related risk factors compared to the general population yet most existing population based studies do not provide specific data for this age-group.

Figure 2: Map of Uganda showing the study districts

Health system provisions for diabetes care: Akin to other districts in Uganda, prevention programs for NCDs at primary care level are scanty. The system for diabetes care in Iganga and Mayuge districts is guided by Uganda's decentrallised public health care system (MOH 2010a), the Uganda's Clinical Guidelines (MOH 2010b), and Guidelines for Non-communicable diseases at the district level (Masaba et al. 1998). These guidelines mostly focus on the person presenting with the classical symptoms of diabetes, by which stage the disease is advanced. Because of this, the management of type 2 diabetes in Uganda and Iganga-Mayuge is based at referral care facilities (HC IV and district hospitals), with lower health units expected to refer the suspected cases. Because services are based at referral facilities, patients often have to travel long distances to receive care. Not all referral facilities in the districts have the capacity to provide diabetes treatment and care. In Iganga district for instance, there is only one public facility that provides diabetes care, the district hospital.

The diabetes clinic in Iganga Hospital runs once a week and currently has 354 patients on follow-up, 201 of whom are women and and 153 are men. It is run by one Clinical Officer and two nurses. Over 60% of patients present with overt symptoms and need insulin. The clinic provides insulin, oral hypoglycaemics and lifestyle education to patients as the key therapies. Drugs are provided for free but with occasional stock-outs, requiring patients to buy them from private pharmacies in Iganga Municipality. Insulin costs approximately US$10 per week. Diabetes patients only get the opportunity to check their blood sugar at the clinic visit. At the start of these studies, there was only one glucometer, with patients paying approximately 2 US$ per test as an out-of-pocket expenditure. The clinic does not provide health education on NCDs to people without diabetes, and neither does the district health team conduct such outreaches. Apart from the single diabetes care centre in the

district, there are a few private-for-profit medical centres in the main town that offer medical treatment for type 2 diabetes. However, their services are often not affordable for the majority of patients. Yet unpublished data also shows that health workers in the two districts have low levels of awareness about diabetes prevention, early diagnosis and treatment.

4.3 STUDY DESIGN AND SAMPLE SELECTION

The overrall study design was a mixed methods approach. Study I and II employed a population-based cross-sectional study design. However, part of the data for study II was secondary data on socio-behavioural characteristics and physical measurements from study I while other data was collected by revisits to households. Study III was a cross-sectional comparative study, nested into Study II. Study III also included a qualitative component using key informants to compare feasibility of two screening tests. Study IV used a qualitative approach, employing Focus Group Discussions.
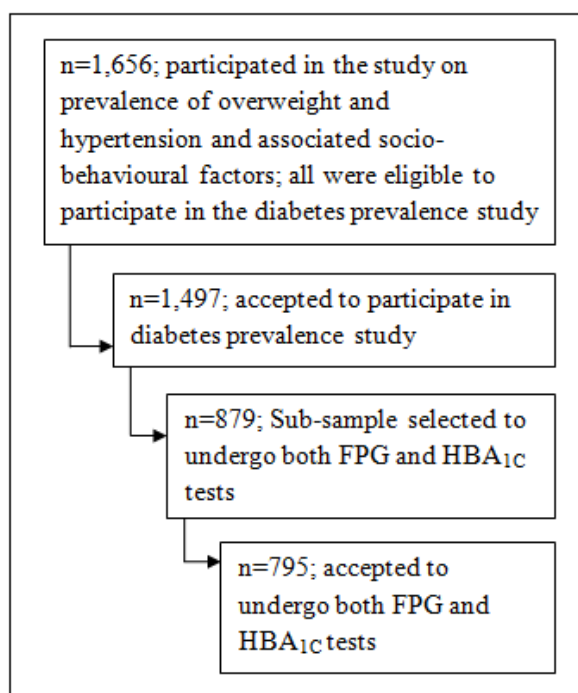
Study I

The sample size was based on the formula for cluster surveys $[C=(Z_\alpha^2 PQ)D /\delta^2 b]$ (Bennett et al. 1991, Kumar and Indrayan 2002): 'Z_α,' the standard normal deviate at 95% confidence, is 1.96; 'P', the prevalence of hypertension, the commonest proximate risk factor for Type 2 diabetes is 23% (Maher et al. 2011); 'D', represents a 'design effect' of 2; 'δ', represents a sampling error of 3% and 'b', the average number of individuals targeted per village was 40. Substituting, a minimum of 38 clusters were needed for the survey, hence a minimum sample size of 1,680, from 42 clusters, inclusive of a 10% adjustment for possible non-response.

A multi-stage sampling strategy was used. The HDSS has a database of all households and household members by village together with their basic demographic characteristics like age and sex. This database is updated every six months. A sample of 42 villages (8 peri-urban and 34 rural) were selected, from which 1,680 target participants were sampled proportionate to the village population sizes, using simple random sampling. HDSS locator information was used to trace sampled participants to their households. 1,656 (98.6%) sampled individuals agreed to participate.

Study II and III

All individuals who participated in study I (1,656) were followed up for inclusion in study II of whom 1,497 agreed to participate (90.4%). Study III was nested into II. The sample size required for comparing differences in prevalence of AGR between FPG and HbA_{1C} was determined using a formula for comparative studies (Fleiss et al. 1980). At a significance level of 95%, power of 80%, estimated prevalence of AGR of 3% (Maher et al. 2011), and hypothesized difference in prevalence of AGR between the two tests at 3%, the minimum computed sample size was 792, adjusted to 879 to cater for 10% estimated non-response. A sub-sample of 879 of the 1,656 participants in the larger study was therefore selected using simple random sampling, of who 795 actually participated (90.4%). A summary of the sample hierarchy for the three quantitative studies is presented in Figure 3 below:

Figure 3: Flow-chart showing the sample hierarchy for study I, II and III

Study IV

Focus group discussions were used, which allowed participants to describe their feelings and perceptions (Wiersma 1995). The FGDs were homogenous with respect to age, sex and type 2 diabetes status. A total of 12 FGDs of eight participants were held. This number of FGDs was selected to enable information saturation and comparison of perspectives from three main categories of participants: people with probable type 2 diabetes (referred to in the rest of the thesis as 'people with diabetes'), people with probable pre-diabetes (referred to as 'people with pre-diabetes') and obese people with normal fasting plasma glucose (referred to as 'obese'), stratified by gender and residence. The cut-offs for defining these glycaemic groups have been defined in the measurements section. We use the term to 'probable' because the test used to classify diabetes (FPG) was non-confirmatory.

The sampling was purposive, targeting three categories of discussants as highlighted. Participants were selected from those who participated in Study II. Using the study II database, three lists were generated by sorting individuals in the three categories. Each list was then stratified into males/females and into rural/peri-urban (to create 12 categories). Eight participants were then selected from each sub-category to make 12 FGDs. HDSS locator information was used to trace the sampled participants to their households. Consenting participants were invited to attend their respective FGD meeting.

4.4 MEASUREMENTS

Study I

Research assistants collected data in two tiers: 1) A questionnaire to assess socio-behavioural characteristics, and 2) physical measurements.

Socio-behavioural variables: A structured questionnaire was used to collect data on socio-behavioural factors including demographic characteristics, socio-economic

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status, family history of diabetes, psychosocial stress, physical activity, tobacco and alcohol use, knowledge about lifestyle-diseases and food frequency. The questionnaire was adapted from different tools that have been validated elsewhere. Most questions were adapted from the WHO Stepwise Approach to NCD Surveillance (STEPS) tool (WHO 2011d), which has been used for risk factor surveillance in some countries in Africa (Guthold et al. 2011). The STEPs tool derives items from other validated tools including the Global Physical Activity Questionnaire (Bull et al. 2009, Papathanasiou et al. 2009, Oyeyemi et al. 2011), questions on alcohol use and smoking (Ustun et al. 1998, Newcombe et al. 2005), questions on psychosocial stress (Eriksson et al. 2008) and the dietary diversity score (Ruel 2003, Savy et al. 2005). Post evaluation of the questions on knowledge about diabetes showed that they had excellent internal consistency (Cronbach's Alpha=82%). The questionnaire was translated into the local language and pre-tested.

Socio-economic status (SES) was assessed using ownership of 11 household assets (UBOS and Macro 2007), following which principal components analysis (PCA) was done. The component on which most assets loaded provided an SES score for each participant. SES scores were then grouped into SES tertiles (UBOS and Macro 2007).

Questions on physical activity assessed participants' undertaking of 'vigorous-intensity activities' and 'moderate-intensity activities' and the time spent on each of these activities in a typical week. Participants were classified into those that met the WHO recommendations of at least 75 minutes of vigorous-intensity, or 150 minutes of moderate-intensity activities per week and those that did not (WHO 2010a).

Tobacco use was assessed using questions on current or ever use of tobacco, whereas alcohol use was assessed with questions on frequency, type and quantity of alcohol consumed. Participants were classified as engaging in 'harmful alcohol use' if they consumed the equivalent of at least 60 grams of pure alcohol either regularly or in a binge in the one month preceding the survey (WHO 2000, WHO 2011f). Information was also collected on family history of diabetes, defined as a history of diabetes in one 1st degree or at least two 2nd degree relatives (Hilding et al. 2006).

Psychosocial stress was measured in five domains (anxiety, apathy, depression, fatigue and insomnia) using five questions adapted from Sweden (Eriksson et al. 2008). The maximum score on this scale was 20. Based on their total score, participants were classified into three stress levels by dividing the range of the scale into three equal parts (0-6=low, 7-13=Moderate, and 14-20=High stress).

Knowledge about lifestyle diseases was measured in five domains using diabetes as a proxy: 1) Awareness about diabetes, 2) its symptoms, 3) its risk factors, 4) its prevention and 5) misconceptions. Participants were scored with a "1" for each item they knew, and with a "0" for those they did not know. The total score for 39 items in the assessment was used to grade participants into two knowledge levels: Inadequate (0-19) and Adequate (20-39) based on the mid-point of the score.

Food frequency was assessed using recall of foods eaten in the previous seven days. Local foods were grouped into nine food groups recommended for dietary diversity assessments (Swindale and Punam 2005). Individual dietary diversity was then assessed by scoring "1" to a food group if the participant had eaten at least one food in that group, or a "0" if they had not (Swindale and Punam 2005). The maximum

possible score was nine. A score of 0-3 was regarded as 'low diversity', 4-6 as 'moderate diversity' and 7-9 as 'high diversity' (Swindale and Punam 2005).

Physical measurements: Height was measured using standard height meters, with the participant standing upright. Weight was measured using calibrated Seca® scales, with the participant lightly clothed. BMI was calculated. A participant was classified as overweight if their BMI was 25 Kgm^{-2} or greater and obese if their BMI was 30 or greater (WHO 1995). Waist and hip circumference were measured using a tape measure. Waist circumference was measured around a horizontal plane through the mid-point between the lower costal margin and the iliac crest, waistline unclothed. Hip circumference was measured around a horizontal plane through the trochanters. To classify abdominal obesity, a normal waist circumference was ≤94 centimetres (cm) for males and ≤80 cm for females, a moderately elevated waist circumference was 94.1-102cm for males and 80.1-88cm for females, and a substantially elevated waist circumference was >102 cm for males and >88cm for females (WHO 1995).

Two blood pressure (BP) measurements were taken (at least 5 minutes apart), with the participant seated, using a calibrated electronic BP device (Welch-Allyn®). The average was calculated to represent their BP. A participant was classified as having hypertension if their average systolic BP was 140mmHg or higher, or if their average diastolic BP was 90mmHg or higher, or if they were on anti-hypertensive treatment (Whitworth 2003). Pre-hypertension was defined as having an average systolic BP between 120 - 139mmHg, or an average diastolic BP between 80 - 89mmHg.

Study II and III

For each participant, Study II and III adopted the same physical and socio-behavioural characteristics that were assessed in Study I. To this was added data on fasting plasma glucose (FPG) (for II and III) and haemoglobin A_{1C} (for III only). Each participant was contacted on the day prior to their scheduled date for data collection and an appointment was sought for the following day. To obtain an FPG, they were requested not to eat anything on the appointment day until their blood test had been conducted. All appointments were set in the morning hours before 10.30am. Participants who had eaten anything on the appointment day were rescheduled.

For each consenting participant a drop of blood was obtained from a finger prick using an automated lancing device and analysed for FPG using a glucometer (On-Call Plus ®, ACON). For the sub-sample of participants in study III, a second drop of blood was analysed for HbA_{1C} using the A1cNow® (Bayer) Rapid Immuno-Assay. Both tests were in form of rapid kits. Point-of-care tests are widely recommended for monitoring of blood glucose and some brands have comparable validity to laboratory-based tests (Little 2005, Shibata K et al. 2005, Lenters-Westra and Slingerland 2010, Wood et al. 2012). Because of their simple procedure, the tests were performed by nurses. From the product's information insert, the Coefficients of Variation (CV) for the On-Call ® Plus test are within acceptable range (less than 10%) for the different plasma glucose values in the range tested. For HbA_{1C}, the new version of A1CNow+ is noted to have better performance through recent introduction of improved manufacturing, improved chemistry and improved calibration (Bode et al. 2007).

Classification of AGR was based on the standard cut-offs for FPG and HbA_{1C} as defined by the ADA (ADA 2013): For FPG, 1) FPG <5.6 mmol/l was classified as normal; 2) FPG >6.9mmol/l was classified as diabetes; 3) FPG between 5.6-6.9 mmol/l was classified as 'pre-diabetes'. All participants with an FPG ≥5.6mmol/l

were classified as having 'AGR'. For HbA$_{1C}$, 1) HbA$_{1C}$ <5.7% (or <39mmol/mol) was classified as having normal glycosylation; 2) HbA$_{1C}$ ≥6.5% (or ≥48mmol/mol) was classified diabetes; 3) HbA$_{1C}$ between 5.7% - 6.4% (39-46mmol/mol) was classified as 'pre-diabetes'. For HbA$_{1C}$, 'AGR' was defined as HbA$_{1C}$ ≥ 5.7% (or ≥39mmol/mol). 'AGR' therefore included both diabetes and pre-diabetes.

Because the WHO has different cut-offs for FPG, a separate cross-analysis between FPG and HbA$_{1C}$ was also conducted using the WHO criteria (III). The WHO cut offs for FPG are (WHO and IDF 2006): 1) FPG <6.1mmol/l (normal); 2) FPG >6.9mmol/l (diabetes); 3) FPG between 6.1 - 6.9mmol/l (pre-diabetes). All participants with an FPG ≥6.1mmol/l were classified as having 'AGR'.

Because the screening tests used in these assessments were all non-confirmatory, all classifications indicated are 'probable'.

Direct medical cost of screening: Study II also estimated the cost of screening all people aged 35-60 years. Using a health services perspective, the direct medical costs of implementing such a program were computed and annualised for one round of health facility-based screening. The main assumption is that all people aged 35-60 years in the district (i.e. 13.5% of an estimated population of 466,200 (Uganda Bureau of Statistics 2007) are offered an FPG test once over a two year period at any visit to a public health facility with laboratory services. The two year period spreads out the costs from salaries and health worker time, which are not included in this analysis. The capital costs include: 1) The price of hand-held Glucometers (one each for 12 health facilities that offer laboratory services in Iganga district, assuming each Glucometer lasts three years); 2) The cost of training health workers (two each for 12 health centres, and assuming that re-training occurs after five years). The recurrent costs include: 1) Costs of the FPG test strips (assuming a wastage rate of 2% as found in this study), and 2) the costs of batteries to power the Glucometers.

Feasibility of FPG and HbA$_{1C}$ rapid tests: Study III assessed feasibility of using the FPG and HbA$_{1C}$ tests in screening. The study nurses were interviewed as key informants, to explore their experiences in using the two tests. Variables included: Ease of use, the test procedure, mistakes, and device error readings and their causes. This information was triangulated with trainers' observations regarding the duration of practice sessions required for research assistants to master the respective test procedures during their training, as well as observational data on the actual duration of each test as recorded during data collection.

Study IV
Two FGDs were held each day. Two moderators asked participants a series of open-ended and probing questions using a prepared FGD Guide. The note-taker audio-recorded the discussions while also taking notes and capturing the expressions. The discussions were held in the Local Council halls at six selected sub-county offices.

To facilitate informed discussion on lifestyles (diet, physical activity and self-monitoring), the moderators used an approach in which participants were told about the biomedical recommendations regarding a particular behaviour and were then asked 'whether they were feasible and how'. This approach is similar to 'motivational interviewing' proposed by Miller and Rollnick, where ambivalent issues are clarified so that the focus is on 'eliciting motivators for change'(Miller and Rollnick 2002).

The FGD guide covered perceptions on five issues: 1) Severity of type 2 diabetes, 2) obesity, 3) healthy diet, 4) physical activity, and 5) self-monitoring of health. These issues were based on a review of articles on recommended lifestyles for prevention on type 2 diabetes (Lagerros and Rossner 2013, Schellenberg et al. 2013). The FGD guide was reviewed by a multi-disciplinary team. It was translated to the local language (Lusoga) and back-translated to English for accuracy.

Methodological approaches to promote validity included follow-up questions and probes, checking repeatedly to ascertain assertions and meanings, and using multiple coders in development of the codebook.

4.5   DATA COLLECTION TEAMS

Study I, II and III
Data were collected by eleven teams, each comprising of two research assistants (a nurse and a social worker). The research assistants underwent three days of rigorous training (Study I) and three additional days of training to implement study II and III.

Study IV
The FGDs were moderated by the principal investigator a (male public health specialist) assisted by an experienced qualitative researcher (also a male). The use of two moderators was to allow sufficient probing. They were supported by a female interpreter and a female note-taker, both conversant with the local language, the former being a nurse and the latter a social scientist.

4.6   DATA MANAGEMENT AND ANALYSIS

Quantitative data (Studies I, II and III)
Data were double entered in EpiData, cleaned and exported to STATA10 for analysis.
Study I
The prevalence of overweight and hypertension was calculated. Logistic regression was used to identify the socio-behavioural factors associated with being overweight and being hypertensive, at a significance level of $p<0.05$. Because waist circumference showed wide disparity between sexes, BMI was used for testing associations. Crude odds ratios (COR), adjusted odds ratios (AOR), and their respective 95% confidence intervals (CI) and p-values are reported. Model fit was evaluated using the Hosmer-Lemeshow test (Hosmer and Lemeshow 2000).

Study II
The prevalence of diabetes and pre-diabetes was calculated. To determine association between AGR and socio-behavioural factors, prevalence rate ratios (PRR) were used rather than odds ratios because the dependent variable (AGR) was highly prevalent. Odds Ratios tend to over-estimate the strength of association in such scenarios (Thompson et al. 1998, Lee et al. 2009). PRRs were estimated using the Modified Poisson regression analysis model, with robust standard errors (Thompson et al. 1998). Unadjusted and adjusted PRRs, plus their confidence intervals (CI) and p-values at $\alpha=0.05$ are presented.

To estimate the cost of detecting one person with AGR, the estimated capital costs of such a program, scaled to the district level, were annualized and added to the estimated recurrent costs for one year to obtain the total annual cost. The cost per person screened was computed. The number of people with AGR that would be detected in one round of a health facility based district-wide screening program

targeting people aged 35-60 years was computed based on the prevalence of AGR in this age-group. Thereafter, the cost of detecting one person with AGR was computed. Using prevalence data for overweight, we also assessed the cost of detecting one person with AGR if screening is targeted only to overweight persons.

Study III

The percentage agreement between the FPG and HBA_{1C} tests in classifying diabetes and AGR was determined at the standard cut-offs and evaluated using the Kappa Statistic. We explored further the predictive value of HbA_{1C} for FPG-defined diabetes status and FPG-defined AGR. The reason for using FPG as the reference was that the data seems to indicate that HbA_{1C} was the less specific test. Percentage agreement was also compared for the two tests among sub-groups with risk factors for type 2 diabetes. Receiver Operating Characteristic (ROC) curves were used to evaluate the performance of HBA_{1C} in predicting FPG-defined diabetes status and AGR.

Qualitative analysis (Study IV)

FGD recordings were transcribed and translated into English by an experienced research assistant fluent in both languages. All authors read the transcripts, and discussed emerging issues. Thereafter three investigators developed a codebook by selecting three transcripts, re-reading them, assigning meaning units to each response and codes to each meaning unit. They then met and unified their codes.

Content analysis was used (Graneheim and Lundman 2004, Nelson et al. 2011). All transcripts were entered into Atlas Ti software. Thereafter, each response was assigned a code. Responses with similar codes were re-categorised under unifying sub-themes and themes, following which the themes were listed. The categories were then interpreted for their descriptive meaning. The authors also identified descriptive quotes representing key themes and an over-arching descriptive theme.

4.7   ETHICAL AND SCIENTIFIC REVIEW

This study was approved by Makerere University School of Public Health Ethics Committee (30th June 2011), the Swedish Regional Ethics Board (Stockholm) (Diary Number 2010/2049-31/2) and the Uganda National Council of Science and Technology. Permission was also obtained from the HDSS management. Each participant consented to be involved, and identification was anonymous.

The main ethical challenge arising out of this study was the required follow-up care for the people with unconfirmed type 2 diabetes, pre-diabetes and hypertension identified in the data collection, since the initial screening tests were not confirmatory. All these participants were referred to Iganga District Hospital's diabetes clinic. A memorandum of understanding was signed with the hospital management and meetings held with the diabetes clinic team to discuss the implications of the additional client load. Additional logistics to facilitate follow-up of the referred participants were provided by the study management to the diabetes clinic. All people suspected to have type 2 diabetes, pre-diabetes or hypertension were provided with counselling about their condition, the need to visit the diabetes clinic for further evaluation, and their lifestyle. They were each given a referral letter in which findings from their preliminary assessment were recorded.

Other ethical challenges arose from a few participants initially denying their results, hence requiring follow-up counselling, participation in multiple studies, requiring

consent for each study and the worry that resulted from telling some participants that they had suspected type 2 diabetes. These challenges were mitigated by providing additional counselling to the affected participants.

4.8   SUMMARY OF THE METHODS

Table 3 below provides a summary of the methods used for the different studies:

Table 3: Summary of the studies and methods used

Design	Timing	Data Collection	Variables	Analysis
I. Cross-sectional population-based *(n=1656; 35-60 years)*	May-June 2011	Physical Measurements	• Height, Weight and BMI • Waist circumference, • Blood Pressure	Prevalence of overweight & hypertension
		Behavioral questionnaire *adapted from validated tools*	• Demographics • 7 Socio-behavioral factors: Family history, stress, Physical activity, Tobacco, Alcohol, Knowledge, Diet	Logistic regression for factors associated with overweight & hypertension
II. Cross-sectional Cluster Survey *(n=1497; Age 35-60)*	March-April 2012	Physical Measurements	• Same as Study I • FPG on appointment after fasting *(On-call Plus, Acon Rapid Kits)*	Prevalence of abnormal glucose regulation (AGR) Un-detected disease
		Behavioral questionnaire	• Same as Study I	Modified Poisson regression for factors associated with AGR
		Costs	• Additional Direct Medical Cost of screening	Cost/person with AGR detected
III. Cross-sectional comparative *(n=795; 35-60; n*ested in II)	March-April 2012	Physical measurements in a sub-sample	• Same as study I • FPG from study II • HbA1c (*A1c Now®*, Bayer AG) • Cut-offs by WHO & ADA	% Agreement in classifying diabetes & hyperglycemia (general and among people with risk factors) ROC: Performance of HbA1c referenced to FPG
		Qualitative	• Feasibility of the two tests	Comparing feasibility

IV. Qualitative; 12 FGDs of 8 people each	May 2013	FGDs of persons with probable diabetes, pre-diabetes and normal but obese persons	• Perceptions on:
			  o Severity of diabetes
			  o Obesity
			  o Healthy diet
			  o Physical activity
			  o Self-monitoring
				Content analysis by a multi-disciplinary team

5 RESULTS

5.1 PREVALENCE OF RISK FACTORS FOR TYPE 2 DIABETES (I)

This section sets the context for understanding type 2 diabetes by showing the extent to which risk factors exist among people aged 35 to 60 years in the community. It also identifies the modifiable risk factors and how these relate with two important risk factors – overweight and hypertension.

Prevalence of overweight, obesity and hypertension in people aged 35-60 years
The mean BMI was 22 (Standard Deviation (SD) = 4.1). Table 4 summarizes key findings on the prevalence of overweight and hypertension by sex:

Table 4: Prevalence of overweight, obesity and hypertension in people aged 35-60 years

Characteristic	Men		Women		Overall	p-value
	n	%	n	%	%	
BMI categories:						
Less than 18.5	142	17.6	124	14.6	16.1	Ref
18.5 – 24.99	585	72.7	513	60.3	66.3	0.975
25 – 29.99	60	7.5	144	16.9	12.3	<0.001
30 +	18	2.2	70	8.2	5.3	<0.001
Waist circumference:						
Normal	755	93.8	455	53.5	73.0	Ref
Moderately elevated	39	4.8	179	21.0	13.2	<0.001
Substantially elevated	11	1.4	217	24.5	13.8	<0.001
Blood pressure:						
Normal or low	214	26.6	339	39.8	33.4	Ref
Pre-hypertensive	424	52.7	339	39.8	46.1	<0.001
Hypertensive or on treatment	167	20.7	173	20.4	20.5	0.356
Both Hypertensive and Overweight:						
No	772	95.9	783	92.0	93.9	Ref
Yes	33	4.1	68	8.0	6.1	0.001
Family history of diabetes						
No	713	88.6	746	87.2	1454	Ref
Yes	92	11.4	110	12.9	202	0.389

Ref=Reference category

Eighteen percent of participants were found to be overweight, with a marked disparity between sexes (25.2% of women vs. 9.7% of men, p<0.001). 5.3% were obese (8.3% of women vs. 2.2% of men, p<0.001) (Table 4). Women were four times more likely to be overweight compared to men (OR 3.7; 95% CI 2.7-5.1). Compared to participants aged 35-39, those aged 45-49 and 50-54 years were more likely to be overweight (OR 1.6; 95% CI 1.1-2.4; OR 1.8; 95% CI 1.1-2.8 respectively). Prevalence of abdominal obesity was 27%, with a much wider disparity between sexes (47% in women vs. 6% in men, p<0.001) (Table 4). A family history of diabetes was found in 12% of participants. Participants with a family history of diabetes were 1.8 times more likely to be overweight (OR 1.8; 95% CI 1.3-2.5).

The prevalence of hypertension was 20.5%, with no difference between sexes (OR 1.0; 95% CI 0.8-1.2). Prevalence of pre-hypertension was 46%. 50% of participants with hypertension were not on treatment. Being hypertensive was associated with age and residence. Compared with the age-group 35-39 years, statistically significant differences in the likelihood of hypertension were observed from the age-group 45-49

years and above. Participants in the age-group 55-60 years were about 5 times more likely to be hypertensive than those in the age-group 35-39 (OR 4.5; 95% CI 2.9-7.0). Peri-urban dwellers were more likely to be hypertensive compared to rural dwellers (OR 2.4; 95% CI 1.6-3.7). Socio-economic status, occupation, level of education and family history of diabetes were not significantly associated with hypertension.

Prevalence of modifiable behavioural risk factors for type 2 diabetes
Table 5 below summarizes key findings on the prevalence of modifiable socio-behavioural characteristics associated with type 2 diabetes.

Table 5: Prevalence of modifiable socio-behavioral risk factors for type 2 diabetes

Characteristic	All (%) n= 1656	By sex				By residence			
		Men (%) n=805	Women (%) n=856	OR	p-Value	Rural (%) n=1352	Peri-Urban n=264	OR	p-Value
WHO physical activity threshold:									
Does not attain	15.9	15.0	14.1	1		9.2	45.5	1	
Attains	84.1	85.0	85.9	1.2	0.612	90.8	54.5	0.1	<0.001
Stress level:									
Low	43.6	47.9	39.6	1		41.9	53.1	1	
Moderate	21.2	32.8	48.9	1.8	<0.001	42.2	35.6	0.7	0.010
High	15.2	19.3	11.6	0.7	0.043	15.9	11.3	0.6	0.013
Knowledge about lifestyle diseases:									
Inadequate	65.4	61.2	69.2	1		66.4	59.9	1	
Adequate	34.6	38.8	30.8	0.7	0.001	33.7	40.1	1.3	0.063
Tobacco user:									
No	94.1	88.3	99.4	1		93.4	98.2	1	
Yes	5.9	11.7	0.6	0.1	<0.001	6.6	1.8	0.3	0.009
Harmful alcohol taker:									
No	95.3	91.6	98.7	1		95.8	92.8	1	
Yes	4.7	8.4	1.3	0.1	<0.001	4.2	7.2	1.8	0.056
Dietary diversity:									
Low	21.6	21.4	21.9	1		19.6	33.3	1	
Moderate	68.2	66.5	69.7	1.0	0.854	70.4	15.4	0.5	<0.001
High	10.2	12.1	8.4	0.7	0.050	10.0	11.3	0.7	0.111

84% of participants met the WHO minimum recommended physical activity threshold. 15% showed high levels of stress. Only 35% had adequate knowledge about lifestyle diseases and only 10% had sufficiently diverse diets (Table 5). The overrall prevalence of smoking and dangerous alcohol taking were very low. Women had significantly less knowledge about lifestyle diseases (OR 0.7; p=0.001) but men were 10 times more likely to smoke and engage in harmful alcohol taking. Men were also more likely to have high stress levels although women predominated in moderate stress. Peri-urban dwellers were more likely not to achieve the recommended physical activity threshold and to engage in harmful alcohol taking compared to rural dwellers. On the other hand, rural residents had less awareness about lifestyle diseases, higher stress levels and higher use of tobacco compared to peri-urban dwellers (Table 5).

Modifiable factors associated with overweight and hypertension
Modifiable socio-behavioural factors found to be associated with being overweight included residence, socio-economic status, hypertension, physical activity, knowledge about diabetes, and dietary diversity. Peri-urban residents were two times more likely to be overweight compared to rural residents (OR 2.1; 95% CI 1.46-3.01). Participants in the highest SES quintile were four times more likely to be overweight

than those in the lowest quintile (OR 4.1; 95% CI 2.4-7.0). Participants who met the WHO minimum threshold for physical activity were significantly less likely to be overweight than those who did not (OR 0.7; 95% CI 0.5-0.9). Participants with moderate dietary diversity were also less likely to be overweight than those with low dietary diversity (OR 0.7; 95% CI 0.5-0.9). Paradoxically, people who knew more about diabetes were more likely to be overweight (OR 2.0; 95% CI 1.0-3.7).

Except for knowledge about life-style diseases and overweight, none of the other modifiable behavioural characteristics were associated with being hypertensive. Stratified analysis shows that not only was there an association between being hypertensive and being overweight (OR 2.5, 95% CI 1.9-3.3), but the association was only statistically significant among rural residents (OR 2.9, p<0.001) and not peri-urban residents (OR 1.3, p=0.363) (p for homogeneity of OR=0.013). Place of residence is therefore an effect-modifier of the relationship between being hypertensive and being overweight. As with BMI, participants who knew more about lifestyle diseases were more likely to be hypertensive.

Summary of key findings

18% of the people aged 35-60 in this predominantly rural setting are overweight. Women were substantially more likely to be overweight and obese compared to men. Overweight is also associated with peri-urban residence, insufficient physical activity and low dietary diversity. About 21% of the people aged 35-60 are hypertensive and 46% have pre-hypertension. 50% of people with hypertension were not on treatment. Hypertension is associated with peri-urban residence, age, and being overweight. Only 35% of participants had comprehensive knowledge about life-style diseases.

With this background information on risk factors, the next step was to assess the prevalence of AGR to clarify its magnitude, its socio-behavioural correlates and the direct medical costs of screening to detect high risk persons.

5.2 PREVALENCE AND CORRELATES OF ABNORMAL GLUCOSE REGULATION (II)

Prevalence of AGR and awareness about diabetes status

The mean FPG value for people aged 35-60 years in this setting was 5.3mmol L^{-1} (Range 2.5-29.9mmol L^{-1}). The prevalence of diabetes was 7.4% (95%CI 6.1-8.8). This included 82 participants with FPG ≥7mmol L^{-1} (5.5%) and 28 on diabetes treatment but with FPG <7.0mmol L^{-1} (1.9%). Using WHO criteria, the prevalence of pre-diabetes was 8.6% (95%CI 7.3-10.2). The ADA cut-offs resulted in a higher prevalence of pre-diabetes (20.2%; 95%CI 17.5-22.9). Prevalence of diabetes and the ratio of diabetes: pre-diabetes increases with increasing 5 year age-categories within the age-group studied but prevalence of AGR levels-off from 50-60 years (Figure 4).
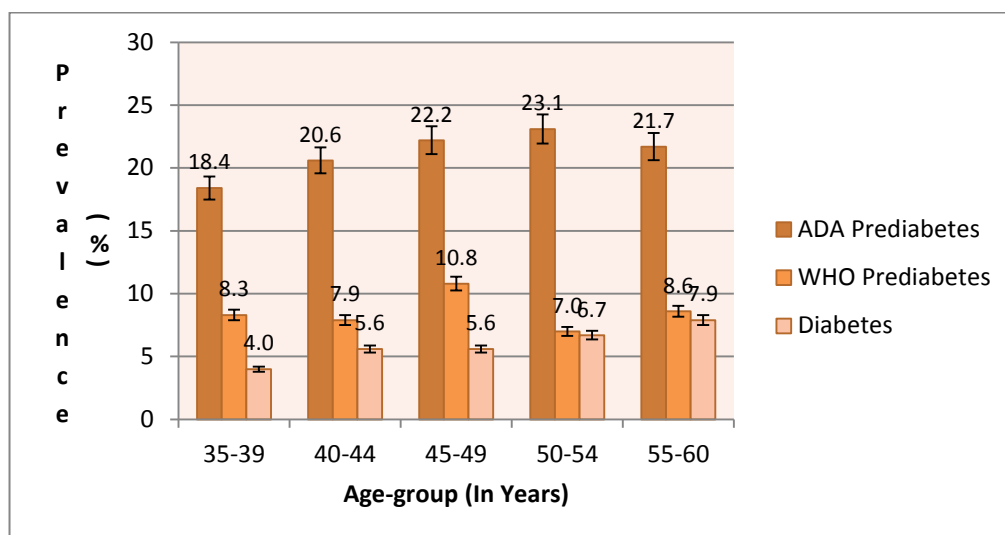
Figure 4: Prevalence of abnormal glucose regulation by age category

Among the 82 participants with FPG levels in the range classified as diabetes, only 16 (19.5%) were aware of their status. Overall, only 44 of the 110 participants (40%) who had diabetes were aware of their status. Among 44 participants on diabetes treatment, only 28 (63.6%) had FPG levels <7 mmol L^{-1}.

Factors associated with AGR among people aged 35-60 years
Table 6 shows factors associated with AGR among people aged 35-60 years.

Table 6: Factors associated with Abnormal Glucose Regulation among people aged 35-60 years

Factor	Category	n	% AGR	PRR	APRR†	P-value
Occupation	Subsistence	171	9.4	1.0	1.0	
	Traders	281	16.4	1.1[0.81-1.50]	1.0[0.75-1.37]	0.932
	Formal salaried	97	19.6	1.3[0.87-2.07]	1.2[0.79-1.94]	0.357
	Mechanic	925	14.6	0.6[0.38-1.02]	0.6[0.37-0.97]	0.038
BMI	18.5-24.9	988	14.2	1.0	1.0	
	<18.5	240	8.8	0.6[0.40-0.95]	0.6[0.40-0.94]	0.027
	25-29.9	189	17.5	1.2[0.87-1.74]	1.2[0.83-1.67]	0.349
	30+	80	27.5	1.9[1.31-2.86]	1.9[1.30-2.83]	0.001
Physical activity	Insufficient	213	21.1	1.0	1.0	
	Attains standard	1261	13.6	0.6[0.48-0.87]	0.6[0.44-0.83]	0.002
Dietary diversity	Low	318	18.2	1.0	1.0	
	Moderate	1005	14.2	0.8[0.59-1.03]	0.8[0.59-1.03]	0.083
	High	151	9.9	0.6[0.32-0.94]	0.5[0.32-0.93]	0.026

PRR=Unadjusted Prevalence Rate Ratio; APRR=Adjusted Prevalence Rate Ratio (†Adjusted for residence, age, occupation, family history of diabetes, BMI, physical activity and dietary diversity)

The prevalence of AGR was twice higher in obese people compared to those with a normal BMI (APRR 1.9, 95% CI 1.3-2.8). AGR did not differ significantly between participants in the overweight category and those with a normal BMI (APRR1.2, 95% CI 0.8-1.7). One in 10 overweight people (11%) and one in five obese people (21%) had diabetes. Sufficient physical activity and higher dietary were associated with a significantly lower likelihood of AGR (APRR 0.6, 95% CI 0.4-0.8; APRR 0.5, 95% CI 0.3-0.9 respectively) (Table 6). While the estimated prevalence of type 2 diabetes

is 5% among people aged 35-60 years, it rises to 12% among those aged 50-54 and averages 7% in the 40 year age-groups.

AGR was significantly lower among people employed as mechanics compared to subsistence farmers (APRR 0.6, 95% CI 0.3-0.9). Further analysis shows that although the majority of our study population achieves the recommended physical activity threshold, substantially more mechanics achieve this threshold (92%) compared with subsistence farmers (80%). Physical activity is therefore an intervening variable in the relationship between occupation and AGR. Although residence was not significantly associated with AGR, adjusting for physical activity resulted in a 40% lower likelihood of AGR among participants from peri-urban villages compared with rural dwellers (APRR 0.6, 95% CI 0.4-0.9). Therefore physical activity is a confounder of the relationship between place of residence and AGR. There was no significant association between sex, age group, level of education, socio-economic status, hypertension, tobacco use and harmful alcohol use with AGR.

Cost per high risk individual discovered through screening
The total annualized direct medical costs of screening all people aged 35-60 years in the district over two years, assuming that 12 health centres are involved, was 16,577 US$. Therefore, the cost per person screened is US$0.53 per year. At the current level of prevalence, the cost of detecting one person with AGR in this age-group is estimated at US$3.7 with WHO criteria and US$2.0 with ADA criteria. If screening is targeted to overweight persons only, the cost of detecting one person with AGR in this age-group is about US$3.0 with WHO criteria and US$1.7 with ADA criteria.

Summary of key findings

> The prevalence of diabetes was 7.4% while pre-diabetes was 9% with WHO and 20% with ADA criteria. 60% of people with suspected diabetes are not aware. At the current level of diabetes prevalence the direct medical cost of screening for AGR in people aged 35-60 is 0.53 US Dollars; the cost per high risk person detected is 2US$ using ADA cut-offs and 3.7 US$ using WHO criteria. Three modifiable factors found to be significantly associated with AGR were being obese, insufficient physical activity and inadequate dietary diversity

Because of the substantial prevalence of AGR in study II, and the high levels of undetected diabetes, further evaluation of the utility of possible screening and diagnostic tools for type 2 diabetes was necessary. Study III therefore assessed the level of agreement between two rapid tests to gauge their utility in this setting.

5.3 UTILITY OF FPG AND HbA$_{1C}$ TESTS IN PRIMARY CARE SCREENING (III)

Agreement between FPG and HbA$_{1C}$ in classifying diabetes status and AGR
There was a marked disparity in AGR prevalence determined by the two tests. FPG classified 4.8% of participants in the range of diabetes while 21.8% and 10.1% were in the range for pre-diabetes (using ADA and WHO criteria respectively). Based on HbA$_{1C}$, 11.3% were in the diabetes range while 26.4% were in the range for pre-diabetes. Table 7 shows the percentage agreement between the two rapid tests:
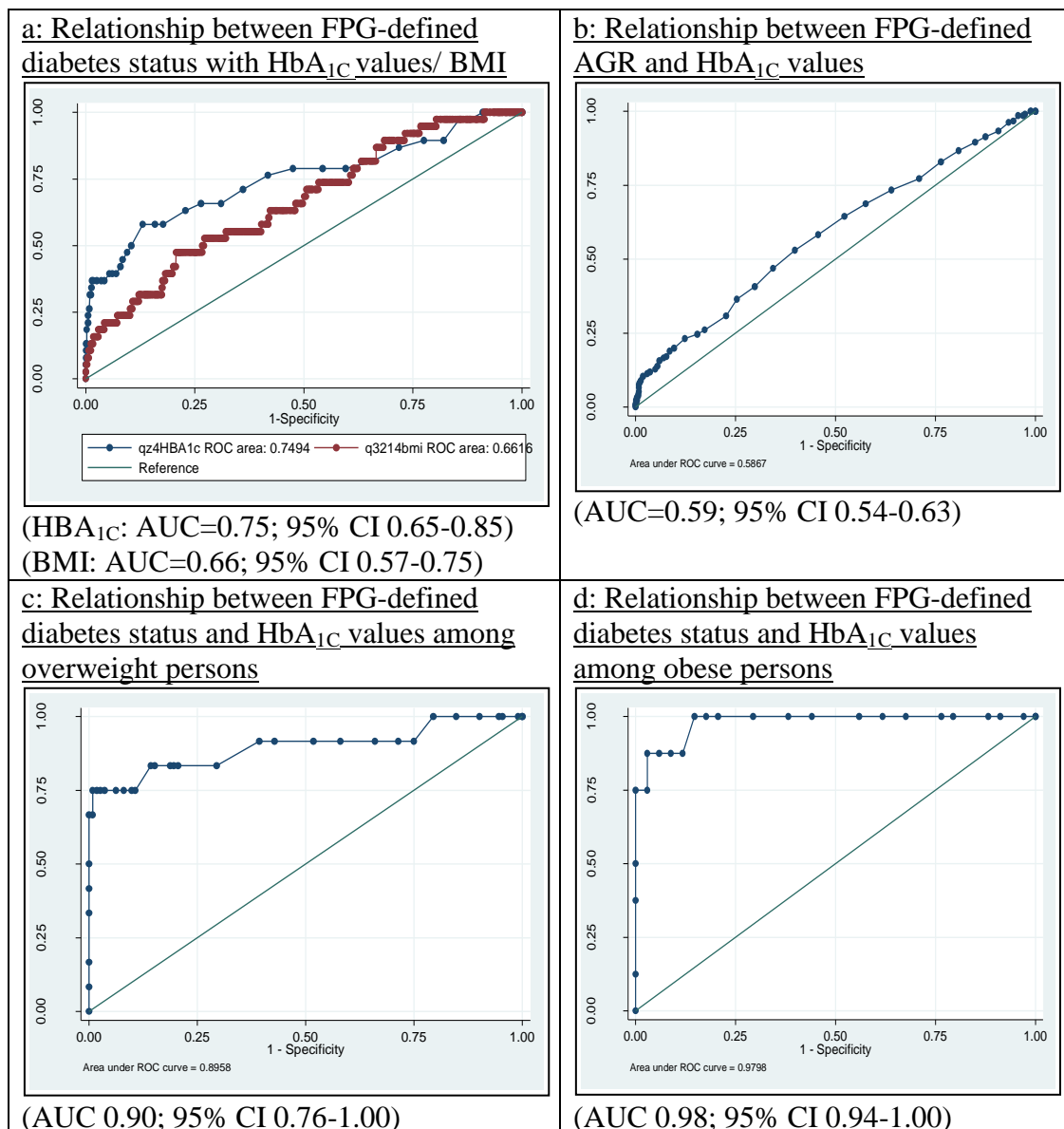
Table 7: Percentage agreement between FPG and HbA_{1c} in classifying diabetes and AGR status

Category	Agreement in classifying diabetes [HBA1c outcomes at given outcomes of FPG]			Agreement in classifying AGR [HBA1c outcomes at given outcomes of FPG]		
	In +Ves	In −Ves	Kappa	In +Ves	In −Ves	Kappa
In the entire sample (n=795)	20%	97%	23%	21%	89%	11%
Among hypertensive (n=159)	28%	99%	35%	21%	94%	14%
Among overweight people (n=124)	39%	98%	45%	28%	87%	14%
Both overweight & hypertensive (n=42)	50%	100%	59%	32%	91%	15%
Among obese persons only (n=42)	62%	100%	69%	48%	100%	43%

Overall agreement between the two rapid tests in classifying diabetes status was low (Kappa=22.9). Agreement was even much lower in classifying AGR (Kappa=10.6% with WHO cut-off and 11.0% with ADA cut-off for FPG). Among persons classified as having diabetes by the FPG test, the HbA_{1C} test provides a similar classification for 53% of them. Likewise, among persons classified as having diabetes by HbA_{1C}, the FPG test only provides a similar classification for 20% (Table 7). Based on the ROC curves, the performance of HbA_{1C} in predicting FPG-defined diabetes status was moderate (AUC=0.75; 95% CI 0.65-0.85) (Figure 5). ROC curve analysis shows that BMI has lower but moderate performance in predicting diabetes-defining FPG levels (AUC=0.66; 95% CI 0.57-0.75) (Figure 5). The same analysis shows that the performance of HbA_{1C} in predicting FPG defined AGR was very low (AUC=0.59; 95% CI 0.54-0.63) (Figure 5). Correlation analysis shows too that although there is substantial linear correlation between the two tests' measurements (p<0.001), the correlation explains a very low threshold of the variability between the two tests (R^2=16%).

Despite the sub-optimal agreement in defining diabetes and AGR, there is high agreement among the negatives. Among persons classified as not having diabetes by the FPG test, the HbA_{1C} test too classifies 91% of them as not having diabetes. Likewise, among persons classified as not having diabetes based on HbA_{1C}, the FPG test too classifies 97% of them as not having diabetes. Similarly, agreement among the negative test results in classifying AGR at given cut-offs for FPG was good (89%).

Similarly, agreement between FPG and HbA_{1C} rapid tests in classifying diabetes status is higher when the tests are conducted among individuals with risk factors for type 2 diabetes. A gradient is observed across risk factors. While a Kappa Statistic of 22.9 is obtained when the two tests are applied to the entire sample, a Kappa of 34.9 is obtained for hypertensive persons, 45.4 for overweight persons, 58.8 for persons who are both overweight and hypertensive and 68.8 for obese persons (Table 7). ROC analysis shows high performance of HbA_{1C} in predicting FPG-defined diabetes status among overweight persons (AUC 0.90; 95% CI 0.76-1.00) and obese persons (AUC 0.98; 95% CI 0.94-1.00) (Figure 5). The strength of the correlation between FPG and HbA_{1C} is higher among people with risk factors (R^2=69% among obese persons). However, agreement between FPG and HbA_{1C} in classifying AGR does not improve among people with risk factors, except in obese people (Kappa=42.9) (Table 7).

a: Relationship between FPG-defined diabetes status with HbA$_{1C}$ values/ BMI	b: Relationship between FPG-defined AGR and HbA$_{1C}$ values
(HBA$_{1C}$: AUC=0.75; 95% CI 0.65-0.85) (BMI: AUC=0.66; 95% CI 0.57-0.75)	(AUC=0.59; 95% CI 0.54-0.63)
c: Relationship between FPG-defined diabetes status and HbA$_{1C}$ values among overweight persons	d: Relationship between FPG-defined diabetes status and HbA$_{1C}$ values among obese persons
(AUC 0.90; 95% CI 0.76-1.00)	(AUC 0.98; 95% CI 0.94-1.00)

Figure 5: Receiver Operating Characteristic (ROC) curves for the relationship between FPG-defined diabetes status and abnormal glucose regulation (AGR) status and HbA$_{1C}$

Feasibility of rapid tests in primary care

According to the research assistants, the devices used in both FPG and HbA$_{1C}$ measurements were easy to use and nurses could administer the tests. The FPG test took a mean of four minutes to perform while the HbA$_{1C}$ test took a mean of nine minutes. Some challenges were observed. For the FPG test, some participants did not comply with fasting, resulting in re-scheduled appointments. The FPG test was also associated with errors but these were reported to be much less frequent compared to HbA$_{1C}$. The HbA$_{1C}$ procedure was viewed as complicated. It required more steps in preparation of the sample. HbA$_{1C}$ also generated more quality control errors than the FPG. It also required precise timing between steps, and a test could be wasted by taking too long or too short between some steps. HbA$_{1C}$ required longer practice before the teams could master the steps. The HbA$_{1C}$ devices failed to operate whenever the room temperature exceeded 28°C, which was common after 11.30 am in Iganga at the time of study III. HbA$_{1C}$ was associated with a 10% wastage rate

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compared to only 2% for the FPG. Other causes of failure of the HbA_{1C} included accidental contamination with moisture and dust. By design, the HbA_{1C} device was tagged to a batch of only 10 tests after which it was auto-disabled.

Summary of key findings

> FPG and HbA_{1C} have moderate agreement in classifying diabetes but low agreement for abnormal glucose regulation. However, their agreement is high among those testing negative with either test, and in people with risk factors for type 2 diabetes especially obese persons. Nurses are capable of administering both rapid tests although FPG is more practical than HbA_{1C}.

Having affirmed that prevalence of type 2 diabetes related risk factors is substantial and that it is possible to identify high risk people using rapid tests or risk factors, it was necessary to know how people with risk factors perceive type 2 diabetes and preventive lifestyles. Study IV therefore explored these perceptions.

5.4 PERCEPTIONS ABOUT DIABETES, OBESITY AND HEALTHY LIFESTYLES (IV)

Perceptions on severity of type 2 diabetes

Participants from the majority of the FGDs viewed type 2 diabetes as a 'very severe disease'. Their explanations were in two main categories: Some said it is severe because it 'cannot be cured' while others cited its consequences to affected people as the reason for its severity. Incurability was qualified by stating that 'it kills' and that it requires 'life-long treatment'.

> *"We know it (diabetes) is a very severe disease. It weakens you and then kills you. It eats you up till you are disabled. I have never seen a person with diabetes who has cured."* (Male FGD, with diabetes, rural)

They explained that people with diabetes require 'injections' before every meal and that they are forbidden from eating some foods like sugar, rice and oil.

> *"Diabetes will require you not to eat certain types of foods.... You always first have to inject yourself then you eat. If you miss treatment for a day, you can even die. Even if you treat it, it can still kill you* (Female FGD, obese, rural)

Among participants who labelled type 2 diabetes as a very severe disease because of its consequences, female participants were concerned about wide-ranging health effects of the disease while male participants were more concerned about the effect of type 2 diabetes on sexual performance, or 'manhood'.

> *"Diabetes leads to many complications including loss of eye sight and heart disease. It makes people weak. They develop pain all the time; they don't get any peace"* (Female FGD, with pre-diabetes, rural)

> *"Diabetes weakens a man's manhood; it reduces sexual performance by making men impotent and infertile. The man no longer satisfies the partner's needs; the wife might run away or engage in extra-marital affairs"* (Male FGD, with diabetes, rural)

Both male and female FGD participants were equally concerned about the economic effects of diabetes including failure to work and expensive long-term treatment.

Views about body weight and obesity
There was a marked difference in perceptions about obesity between FGDs of people with probable type 2 diabetes and those without. Participants with probable type 2 diabetes viewed obesity negatively, associating it with disability and many illnesses.

> *"Before I gained this weight I had no problem; now I have many complications – (high blood) pressure and joint problems. When someone is overweight, her energy and ability reduce. Weight is sickness"* (Female FGD, with diabetes, peri-urban)

However, among participants without diabetes, obesity is associated with wellness: 'eating well', 'high social standing' and 'success'. The local word for an obese person ('omuba') also means 'a very important person'.

> *"In Busoga here when someone is big, they think that person has money. They call them 'omugaiga' (the rich one) or 'Byandaala' (the well-off); if you are a woman, they call you 'Hajjati', a show of respect. When you go to a function or church they give you a front seat"* (Female FGD with pre-diabetes, rural)

Many obese participants said that weight gain is natural and cannot be controlled. Some attributed it to 'having large bones'. Participants from a majority of the FGDs of people without diabetes said that weight loss is stigmatized. When one loses weight, people think he/she is very sick, suffers from HIV or has lost wealth.

> *"If you are big and you lose weight people think you have HIV. When they see someone losing weight they say 'that person is sick'".* (Female FGD, with pre-diabetes, rural)

> *"If you lose weight people think you no longer have money. We now we have micro-finance - people may think that you have failed to pay a loan..."* (Male FGD obese, peri-urban)

Perceptions about healthy diet
To rural participants 'unhealthy foods' mean 'foods that taste sweet, sugary, or contain a lot of sugar', while peri-urban participants cite both sugary foods and 'fried foods' as unhealthy. Peri-urban participants widely believed that as long as meat is only boiled but not fried, its fat content is low. Rural participants also believed that because of their sweet taste, sweet-potatoes are a high risk food, yet they are the staple food in Busoga region.

> *"In Busoga here, one type of food we always eat is sweet potatoes; but they have a lot of sugar and I think they contribute to the high rate of diabetes."* (Male FGD, obese, rural)

Participants were concerned about several barriers to a healthy balanced diet. Some said that cessation of high risk foods is not practical because they have the best taste.

"You see the things they advise us against are also the tastiest - it is difficult to eat un-fried beans. Without sugar or salt, you will not enjoy life" (Female FGD, with pre-diabetes, peri-urban)

Poverty and inability to afford some foods was mentioned as a key barrier to a balanced diet. Protein rich foods were cited as the most expensive. Some participants also linked non-affordability of food to having large families.

"Eating well depends on income; when you have money you can eat chicken, fish and eggs; you cannot buy only half a kilo of meat to serve ten people" (Male FGD, with diabetes, Urban)

Regarding access to food, majority of FGDs said that a range of foods are available in Busoga region in all food categories. However, most FGDs said that it was not possible for households to produce all the necessary foods.

"The main food we grow is sweet potatoes. We face a big problem finding the money to buy other food; we do not have banana or rice plantations. Sometimes all you have is maize flour." (Female FGD, with diabetes, rural)

Several participants said that adjustments for healthy diets are feasible. However, there was a consistent view that 'change involved sacrificing a good life' for a 'controlled' life. 'Eating what one loves' and 'eating tasty food' was viewed as 'having a good life'. Most participants felt that slowly reducing the quantity and frequency of risky foods was more feasible than stopping them abruptly.

"Change means sacrificing a good life... You find problems leaving foods that you enjoy. It is only possible if you reduce slowly." (Male FGD, with pre-diabetes, peri-urban)

Perceptions about physical activity
Participants defined physical activity as 'not sitting in one place' but 'keeping oneself busy'. The majority said that the most feasible form of physical activity was domestic work. The range of possible chores suggested was diverse, including gardening, brick making, tending to domestic animals, fetching water, splitting firewood, bush clearing, and pounding food among rural residents, while washing, cooking, and walking or cycling to the market were cited for peri-urban residents. There was a consistent view that physical activity increments should be nuanced on familiar forms of work.

"Change is possible but in ways familiar to us. Everyone is involved in some domestic work; for me I think the main issue is how much you do…" (Male FGD, with diabetes, rural)

Most participants believe that formal exercises are not feasible for adults in their context, unless they were part of other routine chores or unless someone had diabetes.

"It's impossible for people to wake up and run. Apart from sportsmen, I have never seen anyone leave his home to go running! May be the children - that is the way they behave; but for an adult to run…!" (All laugh) (Male FGD, with pre-diabetes, peri-urban)

Instead, increased walking and cycling were proposed as more feasible alternatives. Several participants said it is feasible to achieve 30 minutes of physical activity daily. However, there was a consistent view that physical activity increments had to be slow because they were not used to them and they meant a major adjustment in their life.

Perceptions about monitoring personal health
Most participants said that it was possible to regularly monitor their health. However, there were different interpretations of how this can be done. Some said they could monitor 'how they feel', and that 'one could feel that he/she is unhealthy'. Others said they could weigh themselves regularly while others said they could go to the health facilities for periodic check-ups. Some barriers to going for health facility check-ups were cited including transport, long distances, work commitments, and not knowing what the check-up entails. Facility related concerns included: waiting times, service charges and uncertainly about whether they would get the service when not ill.

> *"When we are ill, health workers only ask questions and prescribe medications hurriedly without tests; how will they test us when we have no illness?"*(Female FGD, obese, rural)

Participants also expressed the fear of discovering 'health problems' that one could tolerate without knowing them which would lead them to worry.

Summary of key findings

Type 2 diabetes is perceived to be a very severe disease but there are gender differences in explanations: Women were more concerned about the suffering it causes while men were mostly concerned about its effects on sexual performance or 'manhood'. The widespread perception that type 2 diabetes is a severe disease is however in contrast to people's perceptions about preventive measures. Among participants without type 2 diabetes, obesity is associated with 'success' and 'wellness' while weight loss is stigmatised. Adjustment in diet and physical activity are perceived as feasible provided the recommended options are accessible, that changes are introduced gradually, and that proposed activities are familiar to them. Change is perceived as 'sacrificing a good life'.

6 DISCUSSION

This thesis is an exploration of type 2 diabetes in a predominantly rural setting in Uganda. Not only was the prevalence of overweight and hypertension substantial in people aged 35-60years, but rates of abnormal glucose regulation were high, amidst low awareness about lifestyle diseases (I, II). Gender and socio-economic disparities in the distribution of risk factors were observed (I, IV). Obesity, insufficient physical activity and unhealthy diets are highlighted as key correlates of abnormal glucose regulation. The direct medical cost of opportunistic screening for abnormal glucose regulation is US$0.53 per person, translating to US$ 2 per high risk person detected in the age-group studied (II). Although FPG and HbA_{1C} rapid tests have low general agreement in classifying diabetes and abnormal glucose regulation, their convergence is high among people with risk factors and among negative results (III). Communities perceive type 2 diabetes to be a very severe disease, yet they showed low levels of enthusiasm to take up preventive lifestyles. The findings from this study highlight some important options for integration of NCD prevention and care into the health system of a typical low income country.

6.1 RISK FACTORS ARE SUBSTANTIAL AMIDST LOW AWARENESS

The prevalence of overweight and hypertension is substantial among people aged 35-60 years in this predominantly rural setting. One in six people (18%) is overweight (I). Compared with 11% prevalence of overweight reported from a study in rural southern Uganda that included all ages above 12 years (Maher et al. 2011), these findings may imply that people aged 35-60 years are more likely to be overweight than the general population. This could be attributed to higher sedentariness and autonomy over dietary choices in this age-group compared to younger people. However, these rates of overweight and obesity are much lower than those reported in rural South Africa (Bourne et al. 2002), and in many high-income countries (WHO 2011c), probably reflecting an earlier stage in the epidemiological transition.

One in five people (21%) had hypertension (I). Several studies have shown that hypertension occurs frequently in sub-Saharan Africa (Thorogood et al. 2007, Wamala et al. 2009, Oladapo et al. 2010, Maher et al. 2011). The related finding that 46% had pre-hypertension (I) implies a potential for hypertension in this non-elderly age-group to increase. Other risk factors were variable. Obesity (the extreme category of overweight), insufficient physical activity, harmful alcohol taking, and smoking were low while moderate stress and non-diverse diets were frequent (I).

The occurrence of risk factors is not random (I). Socio-demographic factors associated with overweight included sex, residence, age and family history of diabetes, while hypertension was associated with age and peri-urban residence (I). The link between sex and overweight is likely a gender one because several studies show a social desirability of overweight among women in Africa ('big is beautiful') (Maletnlema 2002, Holdsworth et al. 2004, Rguibi and Belahsen 2006, Stern et al. 2010, Lagerros and Rossner 2013). In study I, a gender analysis shows that women had substantially less knowledge about lifestyle diseases, although men were more likely to smoke and engage in harmful alcohol taking (I). Analysis by residence shows that peri-urban dwellers were less physically active and were more likely to engage in harmful alcohol taking compared to rural dwellers. Conversely, rural residents had less knowledge about lifestyle diseases and were more likely to smoke

(I). The modifiable behavioural correlates of overweight were insufficient physical activity and non-diverse diets (I, II). The only modifiable factor found to be associated with hypertension (i.e. being overweight) (I) is insufficient to explain the substantial prevalence of hypertension in this setting.

Only about one third of surveyed individuals had adequate awareness about lifestyle diseases (I). Other studies in Africa have also shown low levels of awareness about healthy lifestyles even among people with chronic diseases (Ike et al. 2010, Donkor et al. 2014). This finding aligns with evidence from study IV which shows gaps in perceptions about risk factors and preventive measures for type 2 diabetes. This situation enhances the urgency for awareness creation on healthy lifestyles. In a context where health education is mainly pre-occupied with acute infectious conditions (Maher et al. 2010, Remais et al. 2013), communities need to be 'awakened' to the reality that type 2 diabetes and related diseases are preventable.

There is critical need for mass awareness raising and behaviour change communication about lifestyle diseases and their risk factors. There is a need to develop health information that effectively links NCD risk factors to disease, and to integrate it into routine health education and promotion activities in primary care. Health information is one of the key health system building blocks, cited too by the WHO as a 'best buy' in population level NCD interventions (WHO 2011c). Traditional health facility- and outreach-based health education sessions would have to be re-oriented and re-organised to integrate education on lifestyle diseases. This includes health education in out-patient clinics, wellness clinics like the child health and family planning clinics, and the routine integrated prevention outreaches. On a larger scale, mass awareness-creation drives using mass media would also be needed so that the level of concern about lifestyle diseases is raised nationally.

The significance of the socio-demographic correlates of overweight and hypertension is that they inform us which sub-populations to target with specific messages. Peri-urban residents and people of higher socio-economic status need targeted education. In addition, messages are needed to change perceptions about obesity in women. The significance of the modifiable risk factors for overweight and hypertension is that they clarify the priority content for behaviour change education, including overweight, hypertension, insufficient physical activity and unhealthy diets (I, II). We also have the opportunity to address smoking and harmful alcohol taking when their prevalence is still low (I).

6.2 HIGH PREVALENCE OF ABNORMAL GLUCOSE REGULATION

Prevalence of abnormal glucose regulation in people aged 35-60 years
There is a high prevalence of abnormal glucose regulation among people aged 35-60 years in this predominantly rural setting (II). 7.4% of people aged 35-60 had probable type 2 diabetes (II), a prevalence estimate that is ten times higher than that observed in another rural setting in southern Uganda (Maher et al. 2011) but the latter survey included a wide age range (≥13 years). Akin to the study in southern Uganda, most previous studies in sub-Saharan Africa have found the prevalence of AGR to be below 2% (Hall et al. 2011) but they too involved wide age ranges including younger participants who are at lower risk of type 2 diabetes. The prevalence of pre-diabetes, the most-at-risk category for type 2 diabetes was 20% using ADA criteria (II), meaning that there are likely three people with pre-diabetes for every person with type 2 diabetes. In the age-group studied, prevalence of AGR peaks between 45-55

years. The expectation therefore that rural areas in low income countries have very low prevalence of AGR and its risk factors is a fallacy if higher risk age-groups are considered (I, II). Nambuya and colleagues found that the mean age of new diabetes patients seen at Uganda's national referral hospital (which mainly serves urban and peri-urban districts in central Uganda) was 45 years while the majority of incident cases were aged 40-49 (Nambuya et al. 1996).

60% of people with blood sugar levels in the range of suspected type 2 diabetes (II) and 50% of those with hypertension (I) were not aware of their status. This finding implies that current diagnostic services are unable to detect the majority of people with type 2 diabetes in its early stages. Nambuya and colleagues showed that almost all new diabetes patients at the national referral hospital in Uganda presented with classical symptoms of diabetes and the majority were severely hyperglycaemic, implying that diagnosis occurs late (Nambuya et al. 1996). However, other settings in sub-Saharan Africa have much higher levels of un-detected diabetes (up to 90%) (Kengne et al. 2013b).

These findings have multiple implications on health information and service delivery, which are requisite components of an NCD responsive health system: Firstly, for countries in earlier stages of the epidemiological transition, crude estimates might mask the high prevalence of abnormal glucose regulation in some higher risk socio-demographic groups. Estimates that are stratified for these groups are therefore necessary in planning NCD interventions because they show whom to target with scarce resources. In low prevalence countries therefore, NCD surveillance data should be disaggregated to show the prevalence in population sub-groups that are likely to be at higher risk – people aged 35-60 are one such group (II).

Secondly, the high prevalence of abnormal glucose regulation (II) and hypertension (I) is further evidence of the need to strengthen secondary care for chronic diseases, including diagnosis, treatment and follow-up. As Uganda's population ages due to increasing life expectancy, the burden of diabetes and CVDs is likely to increase. Because most people with type 2 diabetes are not aware of their status, there is also potential for new diabetes cases seeking care to increase even without an overrall increase in type 2 diabetes prevalence, as people get more aware about the disease. The number of health centres with the capacity to diagnose and treat diabetes and hypertension should be increased. Availability of essential drugs for both diabetes and hypertension (including insulin, oral hypoglycaemic drugs and anti-hypertensive drugs) should be improved. Capacity for follow up care also needs to be developed by availing the logistics to facilitate follow-up of patients and most-at-risk persons, re-organising the existing outpatient services to integrate follow-up activities and re-orienting the health workers on chronic care.

Mass screening would raise major service delivery and ethical challenges
Integration of opportunistic screening for type 2 diabetes in primary care has been widely reviewed but the evidence of its feasibility is equivocal. Many controlled trials show that early detection is efficacious while others show that it is only efficacious when lifestyle interventions are intensive (Janssens et al. 2007, Waugh et al. 2007, Beaglehole et al. 2008, Maher et al. 2010, Allotey et al. 2011). However, translational studies from controlled environments to the 'real world' are lacking (Simmons et al. 2010), more so in sub-Saharan Africa. The value of opportunistic screening for AGR and hypertension in low income countries is therefore uncertain.

Since one quarter of the surveyed population aged 35-60 years in study II was found to have abnormal glucose regulation (II) and one fifth had hypertension (I), mass opportunistic screening for AGR and hypertension is impractical in this setting given that the health system is currently unable to treat, counsel and follow up all the people with risk factors and those with disease that would be identified. The upsurge in new cases in the few health facilities that offer diabetes care would no doubt over-burden them, yet they already face many challenges from under-staffing and lack of essential drugs.

Opportunistic screening would also have implications on health financing, one of the fundamental health system building blocks. According to study II, it costs US$0.53 to screen one person for abnormal glucose regulation, and US$2 to detect one high risk person. Many countries in sub-Saharan Africa cannot afford such costs for one disease condition in a section of the population. Uganda's government spends about US$6 per capita on health (WHO 2009), and an addition of US$0.53 per person aged 35-60 years (13.5% of the population) would translate into a marginal investment of US$0.07 per capita for early detection of type 2 diabetes alone. Moreover, these are direct medical costs only, for one service – screening – and they do not include the costs of lifelong care, out-of-pocket expenditures like transport, clients time and health worker effort. Private expenditure on health in Uganda is estimated at US$24 per capita (WHO 2009) and families may not be capable of taking on additional costs. Mass opportunistic screening also has the potential to disrupt other services.

Instead of mass opportunistic screening for adults, low income countries should consider a two stage risk assessment approach in which only people who fulfil some socio-behavioural risk based criteria undergo more rigorous evaluation with blood tests. Possible first stage evaluation criteria shall be discussed in the next section. However, the utility of mass opportunistic screening would only be fully known if the hidden costs of late detection of type 2 diabetes and hypertension are determined.

6.3   RISK STRATIFICATION

Population approach vs. high risk approach
A key challenge for NCD programs in low income countries is whether to focus on population level measures or the high risk individual. While mass approaches are often needed for mass disease, they offer little benefit to the high risk individual (Rose 1981, Waugh et al. 2007). Conversely, individual approaches would have maximal benefit on the individual but may not impact on population level risk (Rose 1981, Peters 2013). Except for recent evidence from the national cardiovascular risk reduction program in Finland (Rautio et al. 2012), the efficacy of mass population interventions remains equivocal (Johansson et al. 2009, Simmons et al. 2010), yet they are necessary for mass awareness creation. National level regulation of tobacco, alcohol and food has also been highlighted as a best-buy for NCD prevention (WHO 2011c). On the other hand, high risk approaches have been shown to be cost effective in several interventions, when targeted to the most-at-risk persons (Mendis et al. 2004, Waugh et al. 2007). However, most of these studies were conducted in controlled conditions and in high income countries, where the prevalence of risk factors is generally higher than in low income countries.

Study I, II and IV suggest the need to balance both population and high risk approaches. On one hand, the low levels of awareness about lifestyle diseases amidst substantial prevalence of risk factors (I) suggests that mass health education is

necessary. To deal with older most-at-risk persons only would mean ignoring a larger population potentially exposed for several years to lifestyle risks that often start earlier in life and progressively lead to the most-at-risk state. Conversely, the high prevalence of AGR and undetected diabetes (II) suggests the need to strengthen secondary care. To increase awareness while ignoring secondary care would be a recipe for future challenges as the demand for diabetes services increases. 'Most-at-risk approaches' have been increasingly used in HIV prevention in Africa. Innovations that integrate both approaches to increase efficiency should be explored. For example, the substantial numbers of most-at-risk persons and people with diabetes could be turned into a resource, by training them to conduct awareness promotion and risk factor assessment at the community level as they undergo therapy.

The correlates of AGR can guide risk stratification in resource poor settings
Availability of accessible and affordable diagnostics is vital for the health system (Mostafa et al. 2010). Because blood sugar tests are likely to be unaffordable (II), correlates of abnormal glucose regulation can aid in identification of most-at-risk persons for type 2 diabetes who can then under-go further evaluation. Lyon et al argued that in the absence of tools to diagnose early diabetes, health workers could identify proximate risk factors and empirically counsel people on lifestyles (Lyon et al. 2004). Risk scores have been demonstrated to be reliable in predicting disease (Lindstrom and Tuomilehto 2003). However, such 'risk engines' have not been evaluated in sub-Saharan Africa, where some risk factors like smoking and obesity are much less prevalent than in HICs. Studies show that the discriminatory ability of risk scores depends on the context for which they were designed (Buijsse et al. 2011).

Study II identifies three correlates of AGR that could be a starting point in risk assessment: Obesity, insufficient physical activity, and non-diverse diets. 11% of overweight people and 21% of obese people have type 2 diabetes (II). Overweight people from rural areas were also significantly more likely to have hypertension (I). The significance of obesity in predicting AGR is further supported by the findings from ROC analysis (III) which showed that BMI had relatively good correlation with FPG. These correlates could plug an important gap as an aid to risk stratification in the absence of affordable laboratory tests, so that scarce resources are targeted to the most-at-risk groups.

Study I and II also demonstrate the importance of the age threshold of 40 years as a marker for heightened risk for type 2 diabetes and hypertension. Type 2 diabetes prevalence averages 7% between 40-49 years and peaks at 50-54 years (12%). In the age-group studied, inflection in the prevalence curve is noted in the 40-45 year age-band. According to Nambuya and colleagues, the mean age of new diabetes patients seen at Uganda's national referral hospital was 45 years while the majority of new cases were aged 40-49 – this is a relatively young age compared to an average age of 65 years at onset of type 2 diabetes in HICs (Nambuya et al. 1996). These findings, coupled with the increased likelihood of hypertension from 45 years and above suggest a need for closer evaluation of people aged 40 years and over for risk factors.

Based on these observations, it is reasonable to recommend a two-stage risk evaluation approach in primary care settings of low income countries such as Uganda as follows: 1) All people aged 40 years and above should be assessed for overweight and physical activity levels and; 2) based on the first stage of the evaluation, all people aged 40 years and above found to be overweight or to have low physical activity levels should undergo further evaluation for abnormal glucose regulation and

high blood pressure at opportunities when they visit primary care health facilities with the capacity to conduct these assessments. Applying the age and bodyweight threshold as opposed to mass opportunistic screening for all adults would reduce the burden on health facilities by focusing on the most-at-risk people. Targeting the most-at-risk people has also been shown in some studies to be more cost-effective than targeting all people with risk factors (Waugh et al. 2007).

Rapid tests have diagnostic value for type 2 diabetes and utility for screening
Using WHO and ADA criteria, the percentage agreement between FPG and HbA$_{1C}$ rapid tests in classifying diabetes and AGR status is low (III). Similar results were found in Europe (Schottker et al. 2011) and India (Muktabhant et al. 2012) with non-rapid tests. However, study III finds that agreement between FPG and HbA$_{1C}$ in classifying diabetes status is much higher among people with risk factors for type 2 diabetes than the general population. In addition, agreement among the 'negatives' (i.e. those who either test classifies as not having diabetes or AGR) is high independent of whether they have a risk factor, suggesting that the two tests have good specificity (III). These findings show that rapid tests have utility in evaluation of higher risk persons at primary care levels in rural low-income settings. In addition, rapid tests may have value in the diagnosis of type 2 diabetes among people with risk factors (obese, overweight or hypertensive and people with combinations of these). FPG was found to be much more practical in this setting compared to HbA$_{1C}$ (Study III).

Calibration of risk assessment tools for Africa
This thesis raises questions on the utility of several tools for assessment of type 2 diabetes related risk factors in the context of sub-Saharan Africa. Firstly, the marked contrast in the prevalence of pre-diabetes between the WHO and ADA cut-offs for FPG has ethical and service delivery implications. While the lower ADA cut-off is associated with higher screening efficiency (II) (ADA 2013), using it would result in a significantly larger number of high risk people needing long term care (II, III), with consequences on their quality of life, yet the health system is unlikely to accommodate and support all of them. This concern has been raised by the WHO in the guidelines for classification of hyperglycaemia (WHO and IDF 2006). However, this thesis shows that by identifying more most-at-risk persons, the lower ADA cut-off is associated with lower direct medical costs per most-at-risk person detected (II).

Due to the very wide disparity in prevalence of abdominal obesity between men and women (I), the WHO cut-offs for classifying waist circumference may not be appropriate for African women, a concern that has been raised in other studies (Deurenberg 2001, Crowther and Norris 2012). Evidence on the utility of BMI is still equivocal with some authorities arguing that waist circumference is a more reliable marker (Flegal et al. 2013). In study II, 14% of study participants (i.e. 1 in 7) with a normal BMI had AGR, illustrating that BMI is not sufficient to predict the risk of type 2 diabetes. Properly calibrated, waist circumference may be easier to measure by PHC level health workers than BMI which requires multiple measurements and computation.

Because the majority of the study population by definition meets the recommended physical activity threshold, the finding that mechanics had a significantly lower likelihood of AGR than subsistence farmers raises a query on the actual work intensity of subsistence farmers aged 35-60 years in Africa. These findings could imply that subsistence farmers in this age-group are more sedentary than mechanics,

and that self-reported physical activity may be insufficient to evaluate the physical activity levels of subsistence farmers aged 35-60 years in rural low income settings.

The marked disparity in prevalence of AGR as measured by FPG compared to HbA$_{1C}$ (III) supports earlier studies mainly from the United States showing that people of African descent have significantly higher glucose independent glycosylation of haemoglobin than people of Caucasian origin (Ziemer et al. 2010, Selvin et al. 2011). Evidence is also increasingly available that high rates of iron deficiency anaemia could raise HbA$_{1C}$ levels due to yet unconfirmed haematological factors (Hardikar et al. 2012). However, it is also known that FPG has a lower sensitivity than HbA$_{1C}$ (Kumar et al. 2010). FPG levels could also have been generally lowered by the occupational habits of this study population who tend to commence farming work early in the morning. The implication of these findings is that there is need to re-calibrate both the FPG and HbA$_{1C}$ rapid tests for Africa.

6.4   COMMUNITY PERCEPTIONS ABOUT PREVENTIVE LIFESTYLES

Incongruence in community perceptions about type 2 diabetes prevention
While there is a widespread perception that type 2 diabetes is a very severe disease, the same was not reflected in perceptions about preventive lifestyles (IV). Here is a community where people with diabetes view obesity as 'sickness' but the majority without diabetes view obesity as 'a sign of success'. High risk foods are linked to 'enjoyment of life'. Weight loss is stigmatized, a finding highlighted in other studies from Africa (Duda et al. 2006, Rutebemberwa et al. 2013), while some people think that 'weight gain cannot be controlled'. To convince an obese person who feels like she/he is 'having the best of life' to change his/her lifestyle is an enormous challenge, especially in clarifying what constitutes health. In two studies from other settings, obesity was perceived as less risky than smoking (Silagy et al. 1993, Khattab et al. 1999). Others have shown that individuals who are aware about their own risk factors tend to externalize them as not attributed to their own lifestyle (Lucas et al. 2013).

A possible opportunity for health educators in this context is that communities are widely aware of the chronic incurable nature of type 2 diabetes and are concerned about the endless injections and the loss of income due to treatment and cessation of work (IV). Women are very concerned about the pain of diabetes while men are notably concerned about its effects on sexual performance (IV), but all are concerned anyway. These concerns are however not translated into a sense of urgency to change lifestyles as communities emphasize that change should be slow. These findings raise questions about the community's 'notion of health', which appears to be nuanced on current wellness than future health. In at least two other studies, African participants have reported a positive outlook on life that discouraged thought about future sickness (Stern et al. 2010, Cooper et al. 2012). The findings support the need for health information that targets to change the community's notion of health. Health information should empower communities to change their perceptions about obesity and high risk diets and to link healthy choices now to future health gains.

Barriers to lifestyle change
Study participants said they were willing to change their diet, physical activity levels, and monitor their health but change was inhibited by several barriers (IV). Regarding diet, participants said their ability to change is limited by poverty, access to some foods, cost of the food and the large sizes of their families. They said that sugar and cooking oil were difficult to exclude from their diets because of their good taste (IV).

In the rural areas, 'bad sugars' are wrongly associated with sweet potatoes (a staple food) because of their sweet taste. 'Refined foods' like polished rice or maize flour are not cited as unhealthy, despite their increase in rural Africa (Muhihi et al. 2013).

Participants said to too that while they are able to adjust their physical activity levels, they could only do so using familiar forms of activities. Physical activity was viewed as 'informal day-to-day activities' rather than organized exercises. Domestic chores were the preferred platform for increasing their physical activity. The range of chores they suggest are in contrast with preferences among urban residents in Cameroon, who viewed informal physical activities negatively (Kiawi et al. 2006), a discrepancy attributed to the rural-urban difference in context. In two studies in North America, participants too preferred gym work and organized exercise (Miller and Marolen 2012, Bishop et al. 2013) to informal activities, a difference attributed to differences in norms. In the Iganga-Mayuge context, non-familiar activities like running (or jogging) are viewed as 'strange', 'laughable' or 'not suitable for adults' (IV).

These findings clarify some dimensions in behaviour change education messages needed to promote lifestyle change. For behaviour change education to be effective individuals, households and communities need to be offered lifestyle choices that are relevant to their context and within their means. In the context of rural Uganda, messages should emphasize familiar forms of physical activity, with domestic work as the launch platform for increased physical activity. Health educators ought to discuss with individuals, households and communities to identify more accessible alternatives to the expensive high protein foods and other food groups they are not able to access easily.

Study participants feel that it is possible to monitor their health but they had concerns (IV). Regarding seeking health check-ups in health facilities, three of their greatest concerns were the responsiveness of health workers if someone has no ailment, not knowing what the 'check-up' entails, and the fear of unravelling 'what is not known'. These findings resonate with low confidence in health services and other known barriers to access to health services in low income settings (Brenner 2002, Rutebemberwa et al. 2009). With the many competing priorities and shortage of health workers in Uganda's health system, establishment of wellness clinics or outreaches by health workers is likely impractical as it would over-burden an already over-stretched workforce. However, creative ways of empowering individuals to self-assess (e.g. their weight and BMI) may be necessary. Because some of these procedures are relatively simple, assessment procedures like self-weighing can be undertaken by individuals, community health workers and expert clients in their communities or at health facilities, without additional burden to health services.

Behaviour change education
This assessment shows that behaviour change education is required as a key strategy for NCD prevention in low income settings (I, II, IV). Paradoxically, people who were more knowledgeable about lifestyle diseases were also more likely to be overweight (I). Although this may be linked to their higher socio-economic status, it also demonstrates that awareness-creation per-se may not translate into lifestyle change. Therefore, health education should not only create a critical mass of the population that is aware of life-style diseases but it should promote change in lifestyles, both at the individual and the community level. Study IV shows that people afflicted or at higher risk for type 2 diabetes believe that change ought to be slow and requires a major readjustment in what they are used to. Some behaviour change

theories seem to support this notion of phased interventions (Glanz et al. 2008). However, recent meta-analyses do not show convincing evidence of an added benefit from phased interventions (Tuah et al. 2011, Mastellos et al. 2014). Study IV shows that individuals are willing to change behaviour, but they are encumbered by several barriers. To change behaviour therefore, health education ought to go beyond the message to show the individual that change is possible within their means.

An African-centred behaviour change education framework is necessary (BeLue et al. 2009). Based on the findings from this study, health education messages suitable for this context would consist of: 1) Messages about the high burden of type 2 diabetes and abnormal blood sugar levels among people older than 35 years and its implications if no actions are taken (II), 2) messages about the substantial prevalence of risk factors in some population groups (I), linking lifestyle factors to disease and dispelling the normative association of risky lifestyles with success (IV), 3) messages that debunk current misconceptions about health and wellness and link current lifestyles to future health, future quality of life, and lower health care costs (IV), 4) Options regarding physical activity increments that communities are familiar with (e.g. increasing the intensity and duration of domestic work, walking or cycling) or non-familiar activities that they might consider (IV), 5) Overcoming barriers to diet by considering alternatives that are accessible and justifying urgency for change (IV), 6) Addressing gender, rural/urban and socio-economic disparities in risk factors and beliefs about obesity (I, IV), and 7) How individuals can self-monitor some important lifestyle parameters like weight, diet and physical activity and the importance of wellness checks (III,IV). At the individual level, this could involve 'self-persuasion approaches' where individuals are guided to develop their own convictions for changing behaviour (Baldwin et al. 2013). At the community level, the importance of the normative environment in influencing individual behaviour (Ajzen 2011) should be attended to. Modern health education theory supports ecological models that strike a balance between individual behaviours and systems or societal influences (Brenner 2002), as well as 'culturally sensitive' health education that uses 'community own' resources and addresses barriers to change (Netto et al. 2010).

6.5   A NEED FOR 'SMARTER' HEALTH SYSTEMS

The ethics of action and inaction
Study I and II indicate that at least one quarter of the population of people aged 35-60 years are either overweight, have hypertension or have pre-diabetes. A systematic search for all these people and those with un-detected disease is impractical given the current capacity of the health system to provide them with the necessary continuum of quality care to avert progression to disease. Failure to provide services would raise major ethical challenges. For example, the screening activities performed for 1,497 people in study II led to a doubling of clients seeking care at Iganga's only public diabetes treatment clinic. This was because all participants suspected to have diabetes or pre-diabetes based on the screening test were referred to this clinic for further investigation (II). Because this was not part of the clinic's routine, special arrangements had to be made to handle the upsurge in clients. The clinic required more drugs and sundries than their usual need. Negotiations were held with the hospital team and remedial measures were undertaken to provide additional logistics like glucometers, sphygmomanometers, lancets and blood glucose test strips for confirmatory screening. These remedies were possible because the funding for these studies was earmarked. To undertake similar activities in the general health system would result in major logistical constraints, with important ethical implications.

Ethical challenges are also expected to arise from the level of intensity of lifestyle measures prescribed for people with risk factors for type 2 diabetes. Although studies show that pragmatic interventions are much less efficacious than intensive interventions (Simmons et al. 2010), there are recent concerns that in an attempt to achieve rigorous therapeutic targets, people with risk factors are increasingly treated as if they have the disease (Kreiner and Hunt 2013). 'Turning healthy people into chronic patients' substantially reduces their quality of life (Kreiner and Hunt 2013).

On the other hand, low income countries can no longer afford to ignore NCDs on the basis of insufficient resources. The fact that prevalence of risk factors is substantial, the potential for substantial increase in disease burden, and the widespread lack of awareness about lifestyle diseases and their risk factors show that something needs to be done. With awareness creation and behaviour change communication as an option (I), total inaction on the basis of lack of resources is not ethically justifiable.

Restructuring the health system to integrate NCD services
These four studies raise possible options for restructuring the health systems to increase its responsiveness to the rising challenge of NCDs in contexts similar to this. As far as possible, assessment for three key risk factors: overweight, insufficient physical activity, and non-diverse diet needs to be integrated into out-patient services for PHC level facilities, especially targeting people aged 40 years and above. This can be introduced to the lowest level primary care facilities including HC II. People with risk factors should receive health education at the time of assessment. Traditional health education sessions in health facilities should be modified from their current focus on infectious and acute conditions to include wellness and lifestyles, and should also be open to people who are well but with risk factors. Overweight people older than 40 years should be offered further evaluation for abnormal glucose regulation and hypertension. This can be provided at the HC III and above because they have laboratories and clinical staff. People found to have AGR and hypertension would represent the most-at-risk persons and would need behaviour change education. Mechanisms to enhance their adherence to lifestyle change and therapy would need to be put in place including follow-up clinics, community led peer support groups, and the use of expert clients. Along-side these measures should be the implementation of widespread awareness creation on NCDs at the national and sub-national levels, involving stakeholders.

Smarter health systems would be necessary
Suggested actions from this thesis all have implications to the health system, in light of scarce resources. Implementation of individual and community based programs requires a 're-tooling' of primary and secondary care in several health system building blocks. Awareness creation at the community level would require development of context specific messages and disseminating them (Health information) (I). Service packages that include measures for individual level and community level prevention and treatment ought to be developed (Service delivery). Also highlighted is the importance of selective evaluation of people with combinations of risk factors to identify most-at-risk persons. Algorithms and guidelines for risk evaluation and diagnosis would need to be developed (Diagnostics), while the appropriate lifestyle counselling algorithms for most-at-risk persons and medicines for treatment of confirmed people with disease need to be made available (Medicines and therapeutics). Health workers would have to be re-oriented to be able to offer these services (Human resources), while mechanisms for

funding these additional programs would have to be elucidated (Financing). All these actions would require investment of resources at different levels.

The severe shortages of health workers faced by sub-Saharan Africa raise the question of who should provide these services. Major constraints already exist in the efficiency of current primary care (Maher et al. 2010, Mbanya et al. 2010). Many effective interventions for CVD prevention and management are not even affordable or well implemented in high income countries and would be a far cry for the poorest countries (Joshi et al. 2008). However, there is a window of opportunity to prevent the burden of NCDs from reaching its full magnitude as seen in some transitioning countries in Asia (Joshi et al. 2008) by applying measures when the epidemic is in its infancy. This requires the rapid deployment of strategies to curb increase in risk factors. Such strategies need to be tailored for LICs for them to be affordable, effective, and accessible to communities, higher risk groups and people with disease.

Given the many challenges our health systems face, innovations are needed to overcome the obvious challenges regarding financing, human resources, organisation of services, quality, availability of medicines and therapeutics and approaches to health promotion, by elucidation of a viable chronic care model for LICs. These challenges are not new and have been observed in services for acute conditions (Rutebemberwa et al. 2009, Nanyonjo et al. 2012). Integration of additional preventive measures like community education, counselling for people with risk factors and treating the likely increase in number of patients could have a disruptive effect on the already inefficient services. Innovative ways of mobilising community resources to contribute to service provision are needed to offset the increased pressure on formal services. Greater involvement of communities by transferring to them some responsibilities for health education, risk assessment and follow-up of higher risk persons could be explored. In addition, because some risk assessment procedures like assessing obesity, physical activity and diet are simple, service delivery models that empower the high risk individual, expert clients and community health workers to assess them and provide lifestyle counselling could be explored to offset the additional workload to formal health workers.

There is also the potential to learn from HIV treatment programs, a chronic infectious disease for which the health systems of LICs adapted rapidly and in many ways successfully (Whyte 2012), especially regarding detection, initiation of care, follow-up and adherence support (Chalker et al. 2013). HIV programs show that multipronged support systems that employ adherence targets, follow-up appointments, and involvement of community health workers can increase adherence (Agnarson et al. 2010). However, it should be noted that the funding streams for HIV programs have been robust, often involving the mobilisation of resources and the implementation of a progressive agenda at the global and national level. There has also been significant political commitment to these programs by governments in SSA.

Samb and colleagues note that chronic disease interventions could contribute to strengthening the capacity of health systems to deliver a comprehensive range of services and should be a litmus test for health-systems strengthening in LICs (Samb et al. 2010). However, integration of even the basic interventions among those suggested would require substantial re-orientation of the current service delivery paradigm at different levels of the health system (Samb et al. 2010). I have labelled these improved models with the adage 'smart health systems' that can accommodate the concerns of both acute and chronic conditions and 'frugal health systems' that

leverage the potential of existing resources (communities, high risk persons and people with disease) to take charge of the bulk of the NCD agenda.

6.6 METHODOLOGICAL CONSIDERATIONS

Context

All studies (I-IV) were conducted in a HDSS setting, where populations know that they are under observation. However, there were no on-going interventions on NCDs at the population and health facility level in the HDSS which could interfere with the results of these studies.

Measurement of socio-behavioural variables

Methodological challenges were noted in the tools used to measure socio-behavioural variables. The nature of the questions used could have resulted in misclassification biases for key behavioural characteristics like socio-economic status, smoking, dietary diversity, knowledge about lifestyle diseases, physical activity, and stress. Using principal components analysis to assess socio-economic status means that the SES classifications may not be comparable with other populations as the assets common in this population may not be the same elsewhere. The tool used to assess knowledge about lifestyle diseases did not apply weights to the different items but assumed a uniform score per item, yet all items may not signify the same level of knowledge. This could have resulted in over-estimating the level of knowledge. Assessment of physical activity using self-reports could have resulted in over-estimation of physical activity levels. The stress score used in study I was adapted from one used in Sweden and has not been validated in sub-Saharan Africa. It may not have sufficient specificity to stressful situations in sub-Saharan Africa. Using self-reports to assess smoking and alcohol consumption status could have resulted in reporting bias, hence under-counting cases (I, II). In addition, dietary assessment was limited to dietary diversity scores that do not take into account the quantity of nutrients eaten and are liable to recall bias.

These limitations were anticipated and mitigated during study design by as much as possible using validated tools. Principal components analysis is a standard approach that has been used in demographic surveillance in many countries in Africa. The knowledge score used in this analysis was subjected to a reliability analysis and found to have high internal consistency (Cronbach's Alpha=82%). The assessment of physical activity, alcohol taking and smoking were standardised by using validated items that have been employed in other risk factor surveys including in Africa. The items in the stress scale (e.g. anxiety and lack of sleep) are all relevant to the local setting. Diet quality has also been shown in recent studies to have a strong link to cardio-vascular health (Atkins et al. 2014). A full assessment of nutritional food values was outside the scope of this thesis. Hopefully, these considerations mitigated the potential biases in the measurements.

Measurement of physical characteristics

Limitations are noted from using of BMI to assess overweight and obesity and as the dependent variable in testing for associations despite its known shortfalls (I, II, III). BMI is known to be affected by muscle mass and in muscular subjects, is not a good measure of adiposity (Gupta and Kapoor 2014). However, BMI categories have been calibrated and recommended by the WHO as a measure of CVD risk, and are widely used in NCD risk assessments, including the STEPs (WHO 1995). Moreover waist circumference, which could be the alternative dependent variable (I) showed a very

high disparity between sexes and would likely bias the analysis if used instead of BMI. All categorisations (blood pressure, physical activity and BMI) were based on the standard criteria recommended by the WHO.

Blood sugar tests
Study II and III determined AGR on the basis of single rapid FPG and HbA$_{1C}$ tests. Single tests are associated with lower specificity, and a definitive diagnosis of diabetes is based on multiple tests. However, the use of a single test in this study was to evaluate their utility for screening and not for diagnosis. Study II used the FPG test to assess AGR. FPG is recommended by the WHO as the first line screening test for AGR (WHO and IDF 2006). However, it could have led to undercounting of AGR cases as glucose intolerant people with a normal FPG were probably missed. This could have led to a misclassification bias, resulting in some people with AGR being classified as not having it. The effect of this would be to reduce the observed strength of association between the factors assessed and AGR. However, the proportion of glucose intolerant people with a normal FPG is likely to be very low (Hu et al. 2010). Multiple simultaneous tests too are of limited value in screening as their cost would be prohibitive.

The use of rapid tests rather than laboratory based tests could also contribute to misclassification biases. However, misclassifications could affect the results in either way. Current evidence shows that some modern point-of-care tests have comparable accuracy to laboratory based tests including those used in these studies (Little 2005, Lenters-Westra and Slingerland 2010, Wood et al. 2012). In addition the use of rapid tests was purposive because laboratory based tests are more costly for the health system and less accessible to primary care facilities compared to rapid tests.

The Oral Glucose Tolerance Test (OGTT) (which is often used as the gold-standard for diagnosis of type 2 diabetes) was not performed, hence the lack of data on sensitivity and specificity of the tests, and the exclusion of 'Impaired Glucose Tolerance (IGT)' in our comparisons. However, the OGTT would be a cumbersome test to apply to this number of respondents, and has limited value in screening (Anand et al. 2003). There is currently no 'perfect' screening test for early detection of pre-diabetes (Waugh et al. 2007), and all available tests, including the OGTT are to a degree presumptive. In addition there is a lot to learn from a match-up of two tests (FPG and HbA$_{1C}$). Their level of convergence would provide an insight into the implications of their application in a PHC setting. This assessment focused on tests that can be used on a massive scale at PHC levels so as to demonstrate the challenges in their use, as opposed to the more rigorous tests like the OGTT, which may not be applicable as primary care screening tools. Moreover, there have been numerous studies on the sensitivity and specificity of FPG and HbA$_{1C}$ compared to the OGTT and exploring this further might not generate new information.

Another methodological challenge is that HbA$_{1C}$ is known to be affected by haemolysis, haemoglobinopathies, triglycerides, and drugs commonly used in Africa like Aspirin (Kumar et al. 2010, Unnikrishnan and Mohan 2013). This could have explained the high levels of AGR observed with HbA$_{1C}$ compared to FPG. However, most of these confounders tend to lower, rather than increase HbA$_{1C}$ values, except for iron deficiency anaemia which has been recently linked to high HbA$_{1C}$ values. Iron deficiency anaemia is relatively common in rural communities in sub-Saharan Africa, as a result of nutritional factors, gastro-intestinal bleeding, and hookworm infestation.

Cost analysis

Limiting the cost analysis to direct medical costs of a single service (screening) (II) leaves out many other indirect costs, let alone the cost of long term treatment of most-at-risk persons and people with disease that are identified. Study II however only provides preliminary information. Further studies are needed to estimate the longer term benefits of screening with regard to deaths averted and DALYs gained.

Representativeness and generalizability

Overrall, generalizability of the findings of this thesis (all studies) applies to the age-group 35-60 years in a predominantly rural low income setting. This age-group was purposively selected as a possible higher risk group for type 2 diabetes and CVD risk factors, to provide a more focused evaluation, rather than a general population view.

One of the limitations of the qualitative study (IV) is that participants were not on any formal lifestyle programs and were not aware of the recommended behavioural options regarding diet and physical activity. This challenge was mitigated by using a motivational interviewing approach in which participants were educated about the recommended behaviour before asking them to explain whether it was feasible to them. Another consequence of this challenge was that there was no discussion of motivators for change and intensity of lifestyle adjustments but these issues were outside the scope of these studies. Likewise, the categorisation of FGD participants on the basis of blood sugar status likely led to misclassification of some participants, since the test used for this classification (FPG) is not confirmatory. However, the interest in this study was to assess if perceptions were influenced by one's being told his/her suspected risk status, rather than affirmed status. The generalizability of findings in study IV, while not statistical, applies to enriching our understanding by 'zooming in' into context specific perceptions about lifestyle change in settings similar to rural Iganga.

Moderators for the qualitative studies

The limitations of using a lead investigator from a biomedical background are acknowledged. However, the lead investigator had sufficient experience in FGDs, and was supported by an interdisciplinary team. Both the moderator and assistant-moderator were males, with the potential bias that women may not have opened up about their some of their concerns especially regarding sex. This was partly mitigated by using a female interpreter and female notes-taker, and sexuality was not a key research question for this study.

Statistical rigour

Study I employed a logistic regression model. However, because of the relatively frequent prevalence of the key variables assessed, prevalence rate ratios (PRR) would have been more accurate than odds ratios (OR), and a Poisson regression model would have been more accurate. Indeed this approach was used in the regression analysis for study II. Using the Logistic model instead of the Poisson model could have resulted in amplified estimates of the measures of association. Another limitation of this risk based approach is that based on the regression models in study I and II the four factors explained less than 40% of the variability observed.

7 CONCLUSIONS AND RECOMMENDATIONS

1. The prevalence of overweight and hypertension in people aged 35-60 years in this setting is substantial amidst low awareness about lifestyle diseases, hence the need for mass awareness creation about lifestyle-related risk factors (I).

2. There is a high prevalence of abnormal glucose regulation among people aged 35-60 years in this predominantly rural setting, further underpinning the urgency for behaviour change education and strengthening of secondary care (II).

3. Obesity, insufficient physical activity and unhealthy diets were significantly associated with abnormal glucose regulation and could aid in risk stratification at primary care levels (II).

4. Although low in the general sample, agreement between HbA_{1C} and FPG rapid tests is high among people with risk factors for type 2 diabetes and in negative results, with implications for primary care based risk assessment (III).

5. Current cut-offs for available risk assessment measurements (especially waist circumference, HbA_{1C} levels, and FPG cut-offs for pre-diabetes) may not be appropriate for sub-Saharan Africa (I,II, III)

6. Although people at higher risk of type 2 diabetes perceive type 2 diabetes to be a very severe disease, their sense of urgency for uptake of preventive behaviours is low (IV)

7. People aged 35-60 years said that while lifestyle change was practicable, several barriers stood in their way regarding diet, physical activity and self-monitoring; these barriers need to be overcome at individual and household level (IV).

8. Suggestions for strengthening the primary care level response to type 2 diabetes include: mass awareness creation, behaviour change communication on lifestyles, identifying the most-at-risk persons and supporting them to change behaviour, and strengthening capacity for diagnosis and treatment of people with type 2 diabetes (All)

Based on these conclusions, the following recommendations arise:

Mass community health education on type 2 diabetes and NCD risk factors and lifestyles is necessary to avert escalation of risk (I).

Due to the high prevalence of pre-diabetes and hypertension, mass opportunistic screening would be impractical, given the health system constraints of handling an up-surge of high risk persons (II). Overweight, insufficient physical activity and unhealthy diets could be used to identify the most-at-risk persons for type 2 diabetes at primary care levels (II). These should then be selectively evaluated for abnormal glucose regulation and hypertension, given that mass screening is likely not affordable (II). This two-level approach to risk assessment, especially for people aged 40 years and above, is necessary, so that scarce resources are targeted to the most-at-risk persons.

Rapid tests may have diagnostic value for type 2 diabetes among people with risk factors and in screening to identify most-at-risk persons to type 2 diabetes (III). There is however a need for re-calibration of some risk assessment tools to provide more suitable reference ranges for Africa, especially waist-circumference, HbA_{1C}, and the FPG cut-offs for pre-diabetes (I,II, III).

There is need for health information targeting to change the communities' notion of health and wellness. Specifically, messages should change the perceptions that obesity, tasty high risk foods, and sedentariness represent a 'good life' (IV). Health educators should plan with clients on how to overcome barriers to lifestyle change especially in ways familiar to these predominantly rural communities (IV).

Given the gross challenges our health system faces, integration of measures like community education, selective risk evaluation, counselling of high risk people and improved treatment of people with type 2 diabetes require a re-organisation of existing primary care service packages and their delivery mode. Innovative 'smart health systems' that shift some of these responsibilities to affected individuals and communities are needed (All).

8 POLICY IMPLICATIONS

Low income countries like Uganda have an opportunity to address some risk factors for type 2 diabetes when their prevalence is still low (e.g. smoking and obesity), in addition to risk factors that are more frequent (e.g. overweight, hypertension and non-diverse diets). Because prevalence of most-at-risk states (pre-diabetes and pre-hypertension) among people aged 35-60 is substantial, it may not be feasible to massively assess these risk factors at the population level because of the potential burden to the health system. Currently, population level programs to create mass awareness about risk and disease appear more feasible. These activities should be integrated into existing services both at the health facilities and in communities but require a rethinking and re-tooling of the 'integrated prevention package' to include lifestyle change. Likewise, to reduce the workload on health workers, innovative ways of using the 'resources' in communities should be harnessed, as has been done for programs like maternal and new-born health and HIV care. Simple tasks like measuring waist circumference and BMI, as well as counselling of people with risk factors could be shifted to community resource persons and 'expert clients'. Health education paradigms should also change, to balance current and future health concerns, and to change the communities' notion about health and wellness.

The health system implication of the concentration of type 2 diabetes and its risk factors in some population groups is that where population level prevalence is low (typical of low income countries), interventions should incorporate risk stratification, so that the more resource intense activities like lifestyle counselling are targeted to higher risk categories. Since interventions targeting high risk persons have been shown in many studies to be more efficacious in averting progression to disease, the ideal situation would be to periodically screen for pre-diabetes and hypertension among all people aged 35-60 years (mass opportunistic screening). However, given the many challenges that our health system is grappling with, such a program may not be affordable. Rather, selective evaluation of people aged 40-60 that already have some risk factors may be considered, so that scarce resources are targeted to the most-at-risk persons. The preferred PHC level screening test would be FPG, due to its practicality.

Because of the high burden of abnormal glucose regulation, it is imperative that the health systems of low income countries undertake steps to improve secondary care. This should include strengthening diagnosis, treatment and follow-up care. Therefore, in addition to the population level activities, secondary care will have to be strengthened. Service delivery approaches would also have to be re-oriented towards more autonomy for the person with diabetes and the most-at-risk person in taking charge of their health (focus on the patient and the most-at-risk person).

The need to re-calibrate and standardize risk assessment tools for sub-Saharan Africa does not require over-emphasis, especially regarding FPG, HbA1c, BMI and waist circumference. PHC level health workers also need guidelines and job-aids for assessment of socio-behavioural factors including alcohol consumption, smoking, physical activity and diet.

In a health system with minimal PHC level NCD services, challenges on how to handle high risk persons identified through risk assessment need to be addressed.

Effective counselling for such people should include discourse on how to overcome individual and household barriers to lifestyle change. Health educators should also present lifestyle adjustments that are within the options that people are familiar with. Context specific counselling packages that lay out the different barriers and options (both familiar and un-familiar) with regard to diet, physical activity and self-monitoring of health should be developed.

A key question that needs to be answered is: 'should we tamper with NCDs given that a possible increase in demand for NCD services will spiral back into the health system?' Yet we are faced with the reality that we can no longer say that there are no cost effective interventions for prevention and mitigation of NCDs. 'The ethics of inaction' seems to tell us that we need to act now, before NCDs overwhelm the health system. Lastly, a general community approach is inevitable for most countries to create critical awareness about lifestyles and to in-build lifestyle change from the young age, as much as possible using community resources. This requires a critical mass of the population that is aware and sensitised about what to do to improve lifestyles. Community health workers, most-at-risk persons and people with disease are a vast resource that can be used in delivery of prevention and care services for type 2 diabetes.

EPILOGUE

The thesis facilitates a link between diabetology and health systems, illuminating some important issues on health information, service delivery options, and formulation of therapeutic packages for lifestyle education. The suggestions here-in contribute to only part of the health system building blocks. These findings highlight possible options for integration of NCD prevention into the health system of a typical low income country. However the challenges of adding NCD packages to overstretched health systems come to light.

Reflecting on the future: As more evidence emerges on the epidemiology and health system actions to address NCDs and type 2 diabetes in LICs, there is a need to design NCDs service packages based on simple cost-effective interventions. Information generated from these studies shall be used to develop service packages for targeting prevention and treatment of type 2 diabetes. These shall be tested using different service delivery models to determine suitable approaches to roll out the integration of type 2 diabetes and NCD prevention and care in resource constrained settings. Packages should include both individual level and community level interventions. Cost-effectiveness components shall be included to gauge the economic benefits and effectiveness of such service packages.

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10 REFERENCES

Abegunde DO, Mathers CD, Adam T, Ortegon M and Strong K (2007). "The burden and costs of chronic diseases in low-income and middle-income countries." Lancet. **370**(9603): 1929-1938.

Abrahams Z, McHiza Z and Steyn NP (2011). "Diet and mortality rates in Sub-Saharan Africa: Stages in the nutrition transition." BMC Public Health. **11**(1): 801.

ADA (2013). "Standards of medical care in diabetes-2013." Diabetes Care. **36**(Suppl 1): S11-66. doi: 10.2337/dc2313-S2011.

Addo J, Smeeth L and Leon D (2007). "Hypertension in sub-saharan Africa: a systematic review." Hypertension. **50**(6): 1012-1018. Epub 2007 Oct 1022.

Agnarson AM, Masanja H, Ekstrom AM, Eriksen J, Tomson G and Thorson A (2010). "Challenges to ART scale-up in a rural district in Tanzania: stigma and distrust among Tanzanian health care workers, people living with HIV and community members." Trop Med Int Health **15**(9): 1000-1007.

Ajzen I (2011). "The theory of planned behaviour: reactions and reflections." Psychol Health **26**(9): 1113-1127.

Alleyne G, Stuckler D and Alwan A (2010). "The hope and the promise of the UN Resolution on non-communicable diseases." Global Health **6**: 15.

Allotey P, Reidpath DD, Yasin S, Chan CK and de-Graft Aikins A (2011). "Rethinking health-care systems: a focus on chronicity." Lancet. **377**(9764): 450-451. Epub 2010 Nov 2010.

Alwan A, Maclean DR, Riley LM, d'Espaignet ET, Mathers CD, Stevens GA and Bettcher D (2010). "Monitoring and surveillance of chronic non-communicable diseases: progress and capacity in high-burden countries." Lancet **376**(9755): 1861-1868.

Ambady R and Chamukuttan S (2008). "Early diagnosis and prevention of diabetes in developing countries." Rev Endocr Metab Disord. **9**(3): 193-201. Epub 2008 Jul 2007.

Anand SS, Razak F, Vuksan V, Gerstein HC, Malmberg K, Yi Q, Teo KK and Yusuf S (2003). "Diagnostic strategies to detect glucose intolerance in a multiethnic population." Diabetes Care. **26**(2): 290-296.

Angermayr L, Melchart D and Linde K (2010). "Multifactorial lifestyle interventions in the primary and secondary prevention of cardiovascular disease and type 2 diabetes mellitus--a systematic review of randomized controlled trials." Ann Behav Med **40**(1): 49-64.

Atkins JL, Whincup PH, Morris RW, Lennon LT, Papacosta O and Wannamethee SG (2014). "High Diet Quality Is Associated with a Lower Risk of Cardiovascular Disease and All-Cause Mortality in Older Men." J Nutr.

Awah P, Kengne A, Fezeu L and Mbanya J (2008). "Perceived risk factors of cardiovascular diseases and diabetes in Cameroon." Health Education Research **23**(4): 612-620.

Baldwin AS, Rothman AJ, Vander Weg MW and Christensen AJ (2013). "Examining causal components and a mediating process underlying self-generated health arguments for exercise and smoking cessation." Health Psychol **32**(12): 1209-1217.

Beaglehole R, Epping-Jordan J, Patel V, Chopra M, Ebrahim S, Kidd M and Haines A (2008). "Improving the prevention and management of chronic disease in

low-income and middle-income countries: a priority for primary health care." <u>Lancet.</u> **372**(9642): 940-949. doi: 910.1016/S0140-6736(1008)61404-X.

BeLue R, Okoror TA, Iwelunmor J, Taylor KD, Degboe AN, Agyemang C and Ogedegbe G (2009). "An overview of cardiovascular risk factor burden in sub-Saharan African countries: a socio-cultural perspective." <u>Global Health</u> **5**: 10.

Bennett S, Woods T, Liyanage WM and Smith DL (1991). "A simplified general method for cluster-sample surveys of health in developing countries." <u>World Health Stat Q</u> **44**(3): 98-106.

Binnendijk E, Koren R and Dror DM (2012). "Can the rural poor in India afford to treat non-communicable diseases." <u>Trop Med Int Health</u> **17**(11): 1376-1385.

Bischoff A, Ekoe T, Perone N, Slama S and Loutan L (2009). "Chronic disease management in Sub-Saharan Africa: whose business is it?" <u>Int J Environ Res Public Health</u> **6**(8): 2258-2270.

Bishop J, Irby M, Isom S, Blackwell C, Vitolins M and Skelton J (2013). "Diabetes prevention, weight loss, and social support: program participants' perceived influence on the health behaviors of their social support system." <u>Fam Community Health </u>**36** (2): 158-171.

Bode BW, Irvin BR, Pierce JA, Allen M and Clark AL (2007). "Advances in hemoglobin A1c point of care technology." <u>J Diabetes Sci Technol</u> **1**(3): 405-411.

Bodenheimer T, Wagner EH and Grumbach K (2002). "Improving primary care for patients with chronic illness: the chronic care model, Part 2." <u>Jama</u> **288**(15): 1909-1914.

Booth A, Lowis C, Dean M, Hunter S and McKinley M (2013). "Diet and physical activity in the self-management of type 2 diabetes: barriers and facilitators identified by patients and health professionals." <u>Prim Health Care Res Dev.</u> **14**(3): 293-306.

Boruett P, Kagai D, Njogo S, Nguhiu P, Awuor C, Gitau L, Chalker J, Ross-Degnan D, Wahlstrom R and Tomson G (2013). "Facility-level intervention to improve attendance and adherence among patients on anti-retroviral treatment in Kenya--a quasi-experimental study using time series analysis." <u>BMC Health Serv Res</u> **13**: 242.

Bosu WK (2010). "Epidemic of hypertension in Ghana: a systematic review." <u>BMC Public Health.</u> **10**: 418.

Bourne LT, Lambert EV and Steyn K (2002). "Where does the black population of South Africa stand on the nutrition transition?" <u>Public Health Nutr.</u> **5**(1A): 157-162.

Bovet P, William J, Viswanathan B, Madeleine G, Romain S, Yerly P, Paccaud F and Gabriel A (2007) "The Seychelles Heart Study 2004: Methods and main findings ".

Bray G, Look M and Ryan D (2013). "Treatment of the obese patient in primary care: targeting and meeting goals and expectations." <u>Postgrad Med </u>**125**(5): 1941-9260.

Brenner B (2002). "Implementing a community intervention program for health promotion." <u>Soc Work Health Care</u> **35**(1-2): 359-375.

Buijsse B, Simmons RK, Griffin SJ and Schulze MB (2011). "Risk assessment tools for identifying individuals at risk of developing type 2 diabetes." <u>Epidemiol Rev</u> **33**(1): 46-62.

Bull FC, Maslin TS and Armstrong T (2009). "Global physical activity questionnaire (GPAQ): nine country reliability and validity study." <u>J Phys Act Health.</u> **6**(6): 790-804.

Carmoi T, Verret C, Debonne J and Klotz E (2008). "Management of type 2 diabetes in subsaharan Africa: update and perspective." Med Trop (Mars) **67**(6): 601-606.

Chalker JC, Wagner AK, Tomson G, Johnson K, Wahlstrom R and Ross-Degnan D (2013). "Appointment systems are essential for improving chronic disease care in resource-poor settings: learning from experiences with HIV patients in Africa." Int Health **5**(3): 163-165.

Chen KT, Chen CJ, Gregg EW, Imperatore G and Narayan KM (2003). "Impaired fasting glucose and risk of diabetes in Taiwan: follow-up over 3 years." Diabetes Res Clin Pract. **60**(3): 177-182.

Choudhry V, Agardh A, Stafstrom M and Ostergren PO (2014). "Patterns of alcohol consumption and risky sexual behavior: a cross-sectional study among Ugandan university students." BMC Public Health **14**(1): 128.

Cooper M, Harding S, Mullen K and O'Donnell C (2012). "'A chronic disease is a disease which keeps coming back...it is like the flu': chronic disease risk perception and explanatory models among French- and Swahili-speaking African migrants." Ethn Health **17**(6): 597-613.

Cooper RS, Rotimi CN, Kaufman JS, Muna WF and Mensah GA (1998). "Hypertension treatment and control in sub-Saharan Africa: the epidemiological basis for policy." Bmj. **316**(7131): 614-617.

Coronado-Malagon M, Gomez-Vargas JI, Espinoza-Peralta D and Arce-Salinas A (2009). "[Progression toward type-2 diabetes mellitus among Mexican pre-diabetics. Assessment of a cohort]." Gac Med Mex. **145**(4): 269-272.

Crowther NJ and Norris SA (2012). "The current waist circumference cut point used for the diagnosis of metabolic syndrome in sub-Saharan African women is not appropriate." PLoS One **7**(11): e48883.

Dalal S, Beunza JJ, Volmink J, Adebamowo C, Bajunirwe F, Njelekela M, Mozaffarian D, Fawzi W, Willett W, Adami HO and Holmes MD (2011). "Non-communicable diseases in sub-Saharan Africa: what we know now." Int J Epidemiol. **40**(4): 885-901. Epub 2011 Apr 2028.

de-Graft Aikins A, Unwin N, Agyemang C, Allotey P, Campbell C and Arhinful D (2010). "Tackling Africa's chronic disease burden: from the local to the global." Global Health. **6**: 5.

Deurenberg P (2001). "Universal cut-off BMI points for obesity are not appropriate." Br J Nutr. **85**(2): 135-136.

Donkor ES, Owolabi MO, Bampoh P, Aspelund T and Gudnason V (2014). "Community awareness of stroke in Accra, Ghana." BMC Public Health **14**(1): 196.

Duda R, Jumah N, Hill A, Seffah J and Biritwum R (2006). "Interest in healthy living outweighs presumed cultural norms for obesity for Ghanaian women." Health Qual Life Outcomes. **20**(4): 44.

Edelman D, Olsen MK, Dudley TK, Harris AC and Oddone EZ (2004). "Utility of hemoglobin A1c in predicting diabetes risk." J Gen Intern Med. **19**(12): 1175-1180.

Elrayah-Eliadarous H, Yassin K, Eltom M, Abdelrahman S, Wahlstrom R and Ostenson CG (2010). "Direct costs for care and glycaemic control in patients with type 2 diabetes in Sudan." Exp Clin Endocrinol Diabetes **118**(4): 220-225.

Eriksson AK, Ekbom A, Granath F, Hilding A, Efendic S and Ostenson CG (2008). "Psychological distress and risk of pre-diabetes and Type 2 diabetes in a prospective study of Swedish middle-aged men and women." Diabet Med. **25**(7): 834-842.

Eriksson AK, van den Donk M, Hilding A and Ostenson CG (2013). "Work stress, sense of coherence, and risk of type 2 diabetes in a prospective study of middle-aged Swedish men and women." <u>Diabetes Care</u> **36**(9): 2683-2689.

Fezeu L, Minkoulou E, Balkau B, Kengne AP, Awah P, Unwin N, Alberti GK and Mbanya JC (2006). "Association between socioeconomic status and adiposity in urban Cameroon." <u>Int J Epidemiol.</u> **35**(1): 105-111. Epub 2005 Oct 2028.

Flegal KM, Kit BK, Orpana H and Graubard BI (2013). "Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis." <u>Jama</u> **309**(1): 71-82.

Fleiss J, Tytun A and Ury H (1980). "A simple approximation for calculating sample sizes for comparing independent proportions." <u>Biometrics</u> **36**: 343–346.

Geneau R, Stuckler D, Stachenko S, McKee M, Ebrahim S, Basu S, Chockalingham A, Mwatsama M, Jamal R, Alwan A and Beaglehole R (2010). "Raising the priority of preventing chronic diseases: a political process." <u>Lancet</u> **376**(9753): 1689-1698.

Ghatak A, Hazlewood J and Lee T (2008) "How private health care can help Africa." <u>The McKinsey Quarterly</u> **March 2008**.

Gilstrap L, Malhotra R, Peltier-Saxe D, Slicas D, Pineda E, Culhane-Hermann C, Cook N, Fernandez-Golarz C and Wood M (2013). "Community-based primary prevention programs decrease the rate of metabolic syndrome among socioeconomically disadvantaged women." <u>J Womens Health (Larchmt). 2013</u> **22** (4): 322-329.

Glanz K, Rimer B and Visanath K, Eds. (2008). <u>Health Behaviour and Health Education: Theory, Research and Practce</u>, Jossey Bass, A Wiley Imprint 989 Market Street, San Francisco, CA 94103-1741.

Gordis L (2008). <u>Epidemiology</u>, Saunders.

Graneheim U and Lundman B (2004). "Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness." <u>Nurse Educ Today</u> **24** (2): 105-112.

Gupta S and Kapoor S (2014). "Body adiposity index: its relevance and validity in assessing body fatness of adults." <u>ISRN Obes</u> **2014**: 243294.

Guthold R, Louazani SA, Riley LM, Cowan MJ, Bovet P, Damasceno A, Sambo BH, Tesfaye F and Armstrong TP (2011). "Physical activity in 22 African countries: results from the World Health Organization STEPwise approach to chronic disease risk factor surveillance." <u>Am J Prev Med.</u> **41**(1): 52-60.

Hall V, Thomsen RW, Henriksen O and Lohse N (2011). "Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review." <u>BMC Public Health.</u> **11**: 564.

Hardikar PS, Joshi SM, Bhat DS, Raut DA, Katre PA, Lubree HG, Jere A, Pandit AN, Fall CH and Yajnik CS (2012). "Spuriously high prevalence of prediabetes diagnosed by HbA(1c) in young indians partly explained by hematological factors and iron deficiency anemia." <u>Diabetes Care</u> **35**(4): 797-802.

Health Quality Ontario (2009). "Behavioural interventions for type 2 diabetes: an evidence-based analysis." <u>Ont Health Technol Assess Ser</u> **9**(21): 1-45.

Herman WH and Fajans SS (2010). "Hemoglobin A1c for the diagnosis of diabetes: practical considerations." <u>Pol Arch Med Wewn.</u> **120**(1-2): 37-40.

Hilding A, Eriksson AK, Agardh EE, Grill V, Ahlbom A, Efendic S and Ostenson CG (2006). "The impact of family history of diabetes and lifestyle factors on abnormal glucose regulation in middle-aged Swedish men and women." <u>Diabetologia.</u> **49**(11): 2589-2598. Epub 2006 Sep 2513.

Holdsworth M, Gartner A, Landais E, Maire B and Delpeuch F (2004). "Perceptions of healthy and desirable body size in urban Senegalese women." Int J Obes Relat Metab Disord. **28**(12): 1561-1568.

Hosmer D and Lemeshow S (2000). Applied Logistic Regression, Wiley Series in Probability Statistics, John Wiley and Sons Inc.

Hossain P, Kawar B and El Nahas M (2007). "Obesity and diabetes in the developing world--a growing challenge." N Engl J Med. **356**(3): 213-215.

Hu Y, Liu W, Chen Y, Zhang M, Wang L, Zhou H, Wu P, Teng X, Dong Y, Zhou J, Xu H, Zheng J, Li S, Tao T and Jia Y (2010). "Combined use of fasting plasma glucose and glycated hemoglobin A1c in the screening of diabetes and impaired glucose tolerance." Acta Diabetol. **47**(3): 231-236. Epub 2009 Sep 2017.

IDF (2013). World Diabetes Atlas, International Diabetes Federation. **6**.

Ike SO, Aniebue PN and Aniebue UU (2010). "Knowledge, perceptions and practices of lifestyle-modification measures among adult hypertensives in Nigeria." Trans R Soc Trop Med Hyg **104**(1): 55-60.

Janssens B, Van Damme W, Raleigh B, Gupta J, Khem S, Soy Ty K, Vun M, Ford N and Zachariah R (2007). "Offering integrated care for HIV/AIDS, diabetes and hypertension within chronic disease clinics in Cambodia." Bull World Health Organ. **85**(11): 880-885.

Jimeno Mollet J, Molist Brunet N, Franch Nadal J, Morato Griera J, Otzet Gramunt I and Pons Barro P (2004). "Diagnosing type 2 diabetes mellitus: in primary care, fasting plasma glucose and glycosylated haemoglobin do the job." Aten Primaria. **34**(5): 222-228.

Johansson P, Ostenson CG, Hilding AM, Andersson C, Rehnberg C and Tillgren P (2009). "A cost-effectiveness analysis of a community-based diabetes prevention program in Sweden." Int J Technol Assess Health Care **25**(3): 350-358.

Jones AC and Geneau R (2012). "Assessing research activity on priority interventions for non-communicable disease prevention in low- and middle-income countries: a bibliometric analysis." Glob Health Action **5**: 1-13.

Joshi R, Jan S, Wu Y and MacMahon S (2008). "Global inequalities in access to cardiovascular health care: our greatest challenge." J Am Coll Cardiol **52**(23): 1817-1825.

Kengne AP, Echouffo-Tcheugui JB, Sobngwi E and Mbanya JC (2013a). "New insights on diabetes mellitus and obesity in Africa-part 1: prevalence, pathogenesis and comorbidities." Heart **99**(14): 979-983.

Kengne AP, Sobngwi E, Echouffo-Tcheugui JB and Mbanya JC (2013b). "New insights on diabetes mellitus and obesity in Africa-Part 2: prevention, screening and economic burden." Heart **99**(15): 1072-1077.

Khattab MS, Abolfotouh MA, Alakija W, al-Humaidi MA and al-Wahat S (1999). "Risk factors of coronary heart disease: attitude and behaviour in family practice in Saudi Arabia." East Mediterr Health J **5**(1): 35-45.

Kiawi E, Edwards R, Shu J, Unwin N, Kamadjeu R and Mbanya JC (2006). "Knowledge, attitudes, and behavior relating to diabetes and its main risk factors among urban residents in Cameroon: a qualitative survey." Ethn Dis **16**(2): 503-509.

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA and Nathan DM (2002). "Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin." N Engl J Med **346**(6): 393-403.

Koopman RJ, Mainous AG, 3rd, Everett CJ and Carter RE (2008). "Tool to assess likelihood of fasting glucose impairment (TAG-IT)." Ann Fam Med **6**(6): 555-561.

Kreiner M and Hunt M (2013). "The pursuit of preventive care for chronic illness: turning healthy people into chronic patients." Sociology of Health and Illness **Published on line ahead of print**.

Kumar PR, Bhansali A, Ravikiran M, Bhansali S, Dutta P, Thakur JS, Sachdeva N, Bhadada SK and Walia R (2010). "Utility of glycated hemoglobin in diagnosing type 2 diabetes mellitus: a community-based study." J Clin Endocrinol Metab. **95**(6): 2832-2835. Epub 2010 Apr 2836.

Kumar R and Indrayan A (2002). "A nomogram for single-stage cluster-sample surveys in a community for estimation of a prevalence rate." Int J Epidemiol **31**(2): 463-467.

Lachat C, Otchere S, Roberfroid D, Abdulai A, Seret FM, Milesevic J, Xuereb G, Candeias V and Kolsteren P (2013). "Diet and physical activity for the prevention of noncommunicable diseases in low- and middle-income countries: a systematic policy review." PLoS Med **10**(6): e1001465.

Lagerros Y and Rossner S (2013). "Obesity management: what brings success?" Therap Adv Gastroenterol. **6**(1): 77-88.

Lasky D, Becerra E, Boto W, Otim M and Ntambi J (2002). "Obesity and gender differences in the risk of type 2 diabetes mellitus in Uganda." Nutrition. **18**(5): 417-421.

Lee J, Tan CS and Chia KS (2009). "A practical guide for multivariate analysis of dichotomous outcomes." Ann Acad Med Singapore. **38**(8): 714-719.

Lenters-Westra E and Slingerland RJ (2010). "Six of eight hemoglobin A1c point-of-care instruments do not meet the general accepted analytical performance criteria." Clin Chem. **56**(1): 44-52. Epub 2009 Nov 2019.

Lim SS, Gaziano TA, Gakidou E, Reddy KS, Farzadfar F, Lozano R and Rodgers A (2007). "Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs." Lancet **370**(9604): 2054-2062.

Lindeberg SI, Rosvall M, Choi B, Canivet C, Isacsson SO, Karasek R and Ostergren PO (2011). "Psychosocial working conditions and exhaustion in a working population sample of Swedish middle-aged men and women." Eur J Public Health **21**(2): 190-196.

Lindstrom J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, Uusitupa M and Tuomilehto J (2003). "The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity." Diabetes Care. **26**(12): 3230-3236.

Lindstrom J and Tuomilehto J (2003). "The diabetes risk score: a practical tool to predict type 2 diabetes risk." Diabetes Care. **26**(3): 725-731.

Little RR (2005). "Analysis: point-of-care testing for glycated hemoglobin (GHB)." Diabetes Technol Ther. **7**(6): 913-915.

Lopez A, Mathers C, Ezzati M, Jamison D and Murray C (2006). "Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data." Lancet **367**(9524): 1747-1757.

Lucas A, Murray E and Kinra S (2013). "Heath beliefs of UK South Asians related to lifestyle diseases: a review of qualitative literature." J Obes **2013**: 827674.

Lyon AW, Larsen ET and Edwards AL (2004). "The impact of new guidelines for glucose tolerance testing on clinical practice and laboratory services." Cmaj. **171**(9): 1067-1069.

Macisaac RJ and Jerums G (2011). "Intensive glucose control and cardiovascular outcomes in type 2 diabetes." Heart Lung Circ **20**(10): 647-654.

Maher D and Sekajugo J (2011). "Research on health transition in Africa: time for action." Health Res Policy Syst. **9**: 5.

Maher D, Smeeth L and Sekajugo J (2010). "Health transition in Africa: practical policy proposals for primary care." Bull World Health Organ. **88**(12): 943-948. Epub 2010 Nov 2014.

Maher D, Waswa L, Baisley K, Karabarinde A, Unwin N and Grosskurth H (2011). "Distribution of hyperglycaemia and related cardiovascular disease risk factors in low-income countries: a cross-sectional population-based survey in rural Uganda." Int J Epidemiol. **40**(1): 160-171. Epub 2010 Oct 2015.

Maletnlema TN (2002). "A Tanzanian perspective on the nutrition transition and its implications for health." Public Health Nutr. **5**(1A): 163-168.

Masaba J, Baingana S, Odiit A, Nalukenge K and Ofubo L (1998) "Guidelines for non-communicable diseases at District level ".

Mastellos N, Gunn LH, Felix LM, Car J and Majeed A (2014). "Transtheoretical model stages of change for dietary and physical exercise modification in weight loss management for overweight and obese adults." Cochrane Database Syst Rev **2**: Cd008066.

Mbanya J and Ramiaya K (2006) "Disease and Mortality in Sub-Saharan Africa."

Mbanya JC, Motala AA, Sobngwi E, Assah FK and Enoru ST (2010). "Diabetes in sub-Saharan Africa." Lancet **375**(9733): 2254-2266.

Mbanya JC, Motala AA, Sobngwi E, Assah FK and Enoru ST (2010). "Diabetes in sub-Saharan Africa." Lancet. **375**(9733): 2254-2266.

Meigs JB, Muller DC, Nathan DM, Blake DR and Andres R (2003). "The natural history of progression from normal glucose tolerance to type 2 diabetes in the Baltimore Longitudinal Study of Aging." Diabetes. **52**(6): 1475-1484.

Mendis S, Abegunde D, Oladapo O, Celletti F and Nordet P (2004). "Barriers to management of cardiovascular risk in a low-resource setting using hypertension as an entry point." J Hypertens. **22**(1): 59-64.

Mendis S, Lindholm LH, Mancia G, Whitworth J, Alderman M, Lim S and Heagerty T (2007). "World Health Organization (WHO) and International Society of Hypertension (ISH) risk prediction charts: assessment of cardiovascular risk for prevention and control of cardiovascular disease in low and middle-income countries." J Hypertens **25**(8): 1578-1582.

Miller S and Marolen K (2012). "Physical activity-related experiences, counseling expectations, personal responsibility, and altruism among urban African American women with type 2 diabetes." The Diabetes Educator **38**(2): 229-235.

Miller W and Rollnick S (2002). Motivational Interviewing: Preparing People to Change. NY, Guilford Press.

Miranda JJ, Kinra S, Casas JP, Davey Smith G and Ebrahim S (2008). "Non-communicable diseases in low- and middle-income countries: context, determinants and health policy." Trop Med Int Health. **13**(10): 1225-1234.

MOH (2010a). Health Sector Strategic Plan III 2010/11-2014/15. Kampala, Ministry of Health, Uganda.

MOH (2010b). Uganda Clinical Guidelines: Guidelines on management of common conditions.

Mostafa SA, Davies MJ, Webb D, Gray LJ, Srinivasan BT, Jarvis J and Khunti K (2010). "The potential impact of using glycated haemoglobin as the preferred diagnostic tool for detecting Type 2 diabetes mellitus." Diabet Med. **27**(7): 762-769.

Muhihi A, Gimbi D, Njelekela M, Shemaghembe E, Mwambene K, Chiwanga F, Malik V, Wedick N, Spiegelman D, Hu F and Willett W (2013). "Consumption and acceptability of whole grain staples for lowering markers of diabetes risk among overweight and obese Tanzanian adults." Global Health **9(1)** (1): 26.

Muktabhant B, Sanchaisuriya P, Sarakarn P, Tawityanon W, Trakulwong M, Worawat S and Schelp FP (2012). "Use of glucometer and fasting blood glucose as screening tools for diabetes mellitus type 2 and glycated haemoglobin as clinical reference in rural community primary care settings of a middle income country." BMC Public Health **12**: 349.

Nambuya AP, Otim MA, Whitehead H, Mulvany D, Kennedy R and Hadden DR (1996). "The presentation of newly-diagnosed diabetic patients in Uganda." Qjm **89**(9): 705-711.

Nanyonjo A, Nakirunda M, Makumbi F, Tomson G and Kallander K (2012). "Community acceptability and adoption of integrated community case management in Uganda." Am J Trop Med Hyg **87**(5 Suppl): 97-104.

Nelson B, Chung P, DuPlessis H, Flores L, Ryan G and Kataoka S (2011). "Strengthening families of children with developmental concerns: parent perceptions of developmental screening and services in Head Start." Ethn Dis. **21**(3 Suppl 1): S1-89-93.

Netto G, Bhopal R, Lederle N, Khatoon J and Jackson A (2010). "How can health promotion interventions be adapted for minority ethnic communities? Five principles for guiding the development of behavioural interventions." Health Promot Int **25**(2): 248-257.

Newcombe DA, Humeniuk RE and Ali R (2005). "Validation of the World Health Organization Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): report of results from the Australian site." Drug Alcohol Rev. **24**(3): 217-226.

Oladapo OO, Salako L, Sodiq O, Shoyinka K, Adedapo K and Falase AO (2010). "A prevalence of cardiometabolic risk factors among a rural Yoruba south-western Nigerian population: a population-based survey." Cardiovasc J Afr. **21**(1): 26-31.

Omran AR (1971). "The epidemiologic transition. A theory of the epidemiology of population change." Milbank Mem Fund Q **49**(4): 509-538.

Oyeyemi AL, Oyeyemi AY, Adegoke BO, Oyetoke FO, Aliyu HN, Aliyu SU and Rufai AA (2011). "The Short International Physical Activity Questionnaire: cross-cultural adaptation, validation and reliability of the Hausa language version in Nigeria." BMC Med Res Methodol. **11**: 156.

Pan X, Li G, Hu Y, Wang J, Yang W, An Z, Hu Z, Lin J, Xiao J, Cao H, Liu P, Jiang X, Jiang Y, Wang J, Zheng H, Zhang H, Bennett P and Howard B (1997). "Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study." Diabetes Care **20**(4): 537-544.

Papathanasiou G, Georgoudis G, Papandreou M, Spyropoulos P, Georgakopoulos D, Kalfakakou V and Evangelou A (2009). "Reliability measures of the short International Physical Activity Questionnaire (IPAQ) in Greek young adults." Hellenic J Cardiol. **50**(4): 283-294.

Penn L, Dombrowski S, Sniehotta F and White M (2013). "Participants' perspectives on making and maintaining behavioural changes in a lifestyle intervention for type 2 diabetes prevention: a qualitative study using the theory domain framework." BMJ Open **3**(6).

Peters RJ (2013). "[Cardiovascular disease: big problems require big solutions]." Ned Tijdschr Geneeskd **157**(20): A6047.

Probst-Hensch N, Tanner M, Kessler C, Burri C and Kunzli N (2011). "Prevention - a cost-effective way to fight the non-communicable disease epidemic: an academic perspective of the United Nations High-level NCD Meeting." Swiss Med Wkly **141**: w13266.

Rautio N, Jokelainen J, Oksa H, Saaristo T, Peltonen M, Puolijoki H, Tuomilehto J, Vanhala M, Moilanen L, Uusitupa M and Keinanen-Kiukaanniemi S (2012). "Family history of diabetes and effectiveness of lifestyle counselling on the cardio-metabolic risk profile in individuals at high risk of Type 2 diabetes: 1-year follow-up of the FIN-D2D project." Diabet Med **29**(2): 207-211.

Rautio N, Jokelainen J, Polonen A, Oksa H, Peltonen M, Vanhala M, Puolijoki H, Moilanen L, Tuomilehto J, Uusitupa M, Keinanen-Kiukaanniemi S and Saaristo T (2014). "Changes in lifestyle modestly reduce the estimated cardiovascular disease risk in one-year follow-up of the Finnish diabetes prevention program (FIN-D2D)." Eur J Cardiovasc Nurs.

Remais JV, Zeng G, Li G, Tian L and Engelgau MM (2013). "Convergence of non-communicable and infectious diseases in low- and middle-income countries." Int J Epidemiol **42**(1): 221-227.

Rguibi M and Belahsen R (2006). "Fattening practices among Moroccan Saharawi women." East Mediterr Health J **12**(5): 619-624.

Robinson HM and Hort K (2012). "Non-communicable diseases and health systems reform in low-and-middle-income countries." Pac Health Dialog **18**(1): 179-190.

Roglic G and Unwin N (2010). "Mortality attributable to diabetes: estimates for the year 2010." Diabetes Res Clin Pract **87**(1): 15-19.

Rose G (1981). "Strategy of prevention: lessons from cardiovascular disease." Br Med J (Clin Res Ed) **282**(6279): 1847-1851.

Ruel MT (2003). "Is dietary diversity an indicator of food security or dietary quality? A review of measurement issues and research needs." Food Nutr Bull. **24**(2): 231-232.

Rutebemberwa E, Kallander K, Tomson G, Peterson S and Pariyo G (2009). "Determinants of delay in care-seeking for febrile children in eastern Uganda." Trop Med Int Health **14**(4): 472-479.

Rutebemberwa E, Katureebe S, Gitta S, Mwaka A and Atuyambe L (2013). "Perceptions of diabetes in rural areas of Eastern Uganda." Curationis **36**(1).

Rutebemberwa E, Pariyo G, Peterson S, Tomson G and Kallander K (2009). "Utilization of public or private health care providers by febrile children after user fee removal in Uganda." Malar J **8**: 45.

Samb B, Desai N, Nishtar S, Mendis S, Bekedam H, Wright A, Hsu J, Martiniuk A, Celletti F, Patel K, Adshead F, McKee M, Evans T, Alwan A and Etienne C (2010). "Prevention and management of chronic disease: a litmus test for health-systems strengthening in low-income and middle-income countries." Lancet **376**(9754): 1785-1797.

Savy M, Martin-Prevel Y, Sawadogo P, Kameli Y and Delpeuch F (2005). "Use of variety/diversity scores for diet quality measurement: relation with nutritional status of women in a rural area in Burkina Faso." Eur J Clin Nutr. **59**(5): 703-716.

Schellenberg E, Dryden D, Vandermeer B, Ha C and Korownyk C (2013). "Lifestyle Interventions for Patients With and at Risk for Type 2 Diabetes: A Systematic Review and Meta-analysis." Ann Intern Med. **159**(8): 543-551.

Schottker B, Raum E, Rothenbacher D, Muller H and Brenner H (2011). "Prognostic value of haemoglobin A1c and fasting plasma glucose for incident diabetes and implications for screening." Eur J Epidemiol. **26**(10): 779-787. Epub 2011 Sep 2027.

Seedat YK (2007). "Impact of poverty on hypertension and cardiovascular disease in sub-Saharan Africa." Cardiovasc J Afr. **18**(5): 316-320. Epub 2007 Oct 2022.

Selvin E, Steffes MW, Ballantyne CM, Hoogeveen RC, Coresh J and Brancati FL (2011). "Racial differences in glycemic markers: a cross-sectional analysis of community-based data." Ann Intern Med. **154**(5): 303-309. doi: 310.1059/0003-4819-1154-1055-201103010-201100004.

Sensasi B (2006) "Draft Non Communicable Diseases Protocol; for the World Health Organization, Uganda Country Office."

Shaw JE, Sicree RA and Zimmet PZ (2010). "Global estimates of the prevalence of diabetes for 2010 and 2030." Diabetes Res Clin Pract. **87**(1): 4-14. Epub 2009 Nov 2006.

Shibata K, Suzuki S, Sato J, Ohsawa I, Goto S, Iritani I and S T (2005). "Diagnostic accuracy of glycohemoglobin A1c (HbA1c) for postprandial hyperglycemia was equivalent to that of fasting blood glucose. ." Journal of Clinical Epidemiology **Volume: 58**(Issue: 10): Pages: 1052-1057:.

Silagy C, Muir J, Coulter A, Thorogood M and Roe L (1993). "Cardiovascular risk and attitudes to lifestyle: what do patients think?" Bmj **306**(6893): 1657-1660.

Simmons RK, Unwin N and Griffin SJ (2010). "International Diabetes Federation: An update of the evidence concerning the prevention of type 2 diabetes." Diabetes Res Clin Pract **87**(2): 143-149.

Stern R, Puoane T and Tsolekile L (2010). "An exploration into the determinants of noncommunicable diseases among rural-to-urban migrants in periurban South Africa." Prev Chronic Dis **7**(6): A131.

Strong K, Mathers C, Epping-Jordan J and Beaglehole R (2006). "Preventing chronic disease: a priority for global health." Int J Epidemiol. **35**(2): 492-494. Epub 2006 Jan 2030.

Stuckler D and Siegel K, Eds. (2011). Sick Societies: Responding to the global challenge of chronic disease, Oxford Univer, Oxford University Press Inc., New York.

Subramanian SV, Perkins JM and Khan KT (2009). "Do burdens of underweight and overweight coexist among lower socioeconomic groups in India?" Am J Clin Nutr **90**(2): 369-376.

Swindale A and Punam O-V (2005). Measuring Household Food Consumption: A Technical Guide, Food and Nutrition Technical Assistance (FANTA) Project, Academy for Educational Development (AED).

Thompson ML, Myers JE and Kriebel D (1998). "Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: what is to be done?" Occup Environ Med. **55**(4): 272-277.

Thorogood M, Connor M, Tollman S, Lewando Hundt G, Fowkes G and Marsh J (2007). "A cross-sectional study of vascular risk factors in a rural South African population: data from the Southern African Stroke Prevention Initiative (SASPI)." BMC Public Health. **7**: 326.

Tuah NA, Amiel C, Qureshi S, Car J, Kaur B and Majeed A (2011). "Transtheoretical model for dietary and physical exercise modification in weight loss management for overweight and obese adults." Cochrane Database Syst Rev(10): Cd008066.

UBOS and Macro (2007). Uganda Demographic and Health Survey 2006. M. Calverton, USA: UBOS and Macro International Inc. August 2007 UBOS and Macro International Inc.**:** 19-20.

Uganda Bureau of Statistics (2007) "Projections of demographic trends in Uganda 2007-2017." **1**.

UN Inter-Agency Group (2013) "Levels and Trends in Child Mortality: Report 2013."

Unnikrishnan R and Mohan V (2013). "Challenges in estimation of glycated hemoglobin in India." Diabetes Technol Ther. **10**(1557-8593 (Electronic)): 897-899.

Unwin N and Alberti KG (2006). "Chronic non-communicable diseases." Ann Trop Med Parasitol. **100**(5-6): 455-464.

Ustun B, Compton W, Mager D, Babor T, Baiyewu O, Chatterji S, Cottler L, Gogus A, Mavreas V, Peters L, Pull C, Saunders J, Smeets R, Stipec MR, Vrasti MRS, Hasin D, Room R, Van den Brink W, Regier D, Blaine J, Grant BF and Sartorius N (1998). "WHO Study on the reliability and validity of the alcohol and drug use disorder instruments: Overview of methods and results (vol 47, pg 161, 1997)." Drug and Alcohol Dependence **50**(2): 185-186.

Waiswa P, Kallander K, Peterson S, Tomson G and Pariyo GW (2010). "Using the three delays model to understand why newborn babies die in eastern Uganda." Trop Med Int Health **15**(8): 964-972.

Wamala JF, Karyabakabo Z, Ndungutse D and Guwatudde D (2009). "Prevalence factors associated with hypertension in Rukungiri district, Uganda--a community-based study." Afr Health Sci. **9**(3): 153-160.

Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, Williams R and John A (2007). "Screening for type 2 diabetes: literature review and economic modelling." Health Technol Assess. **11**(17): iii-iv, ix-xi, 1-125.

Weinehall L, Hellsten G, Boman K and Hallmans G (2001b). "Prevention of cardiovascular disease in Sweden: the Norsjo community intervention programme--motives, methods and intervention components." Scand J Public Health Suppl **56**: 13-20.

Weinehall L, Lewis C, Nafziger AN, Jenkins PL, Erb TA, Pearson TA and Wall S (2001a). "Different outcomes for different interventions with different focus!-- A cross-country comparison of community interventions in rural Swedish and US populations." Scand J Public Health Suppl **56**: 46-58.

Whitworth JA (2003). "2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension." J Hypertens. **21**(11): 1983-1992.

WHO-AFRO (2011) "Health Situation in the Africa Region: Atlas of Health Statistics 2011."

WHO (1995). Physial Status: The Use and Interpretation of Anthropometry: Report of a WHO Expert Committee. WHO.

WHO (2000). International Guide for Monitoring Alcohol Consumption and Related Harm, Department of Mental Health and Substance Dependence Noncommunicable Diseases and Mental Health Cluster, World Health Organization.

WHO (2007) "Everybody's business: Stregthening health systems to improve health outcomes: WHO's framework for action."

WHO (2009) "World Health Statistics: Health Expenditure."

WHO (2010a). Global Recommendations on Physical activity for Health, WHO, Geneva.

WHO (2010b) "Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-Resource Settings."

WHO (2011a) "The Abuja Declaration: 10 Years On."

WHO (2011b). Global Atlas on cardiovascular disease prevention and control. P. P. a. B. N. Shanthi Mendis. 2011, World Health Organization in collaboration with the World Heart Federation and the World Stroke Organization.

WHO (2011c). Global status report on noncommunicable diseases 2010: Description of the global burden of NCDs, their risk factors and determinants. WHO.

WHO (2011d). STEPS Manual, STEPS Instrument. WHO, WHO.

WHO (2011e) "Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus. Abbreviated Report of a WHO Consultation 2011."

WHO (2011f) "Global Status Report on Alcohol and Health." 16.

WHO (2013) "World Malaria Report 2013."

WHO and IDF, Eds. (2006). Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation.

Whyte SR (2012). "Chronicity and control: framing 'noncommunicable diseases' in Africa." Anthropology and Medicine(1469-2910 (Electronic)).

Wiersma W (1995). Research methods in education : an introduction, Allyn and Bacon**:** 211-212.

Wilson SE, Lipscombe LL, Rosella LC and Manuel DG (2009). "Trends in laboratory testing for diabetes in Ontario, Canada 1995-2005: a population-based study." BMC Health Serv Res. **9**: 41.

Wood JR, Kaminski BM, Kollman C, Beck RW, Hall CA, Yun JP, Cengiz E, Haller MJ, Hassan K, Klingensmith GJ and Tamborlane WV (2012). "Accuracy and precision of the Axis-Shield Afinion hemoglobin A1c measurement device." J Diabetes Sci Technol. **6**(2): 380-386.

Yoon U, Kwok L and Magkidis A (2013). "Efficacy of lifestyle interventions in reducing diabetes incidence in patients with impaired glucose tolerance: a systematic review of randomized controlled trials." Metabolism **62**(2): 303-314.

Ziemer DC, Kolm P, Weintraub WS, Vaccarino V, Rhee MK, Twombly JG, Narayan KM, Koch DD and Phillips LS (2010). "Glucose-independent, black-white differences in hemoglobin A1c levels: a cross-sectional analysis of 2 studies." Ann Intern Med. **152**(12): 770-777.