Derivation and Validation of a Simple Risk Score for Undiagnosed Diabetes for Tanzania and Other African Populations

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Abstract

Background Diabetes prevalence is increasing worldwide. Increased burden of diabetes and recent developments in treatment and prevention of diabetes and cardiovascular complications present opportunities for screening of people at risk of diabetes in order to implement disease-modifying intervention and prevent long-term complications.

Aim The aim of this study was to develop a simple inexpensive score for identifying individuals with undiagnosed diabetes in the African context.

Methods A population based sample of 5193 individuals aged 15 years and above from diabetes surveys in Tanzania, Senegal and Guinea was used to develop the score, the derived score was then validated in populations from South Africa, Guinea and Tanzania. New cases of diabetes were defined using fasting glucose measurements. Binary logistic regression model coefficients were used to assign individual scores for the predictor variables in the model.

Results Age, hypertension and waist circumference were the variables included in the final model. The model has an area under the ROC curve (AUC) of 0.83 (95% CI 0.82 to 0.84). A meta-analysis of applying the score at individual country data yielded a summary ROC curve with an AUC of 0.8 (95% CI 0.74-0.85) and an inconsistency score (I^2) of 0%. The performance of the newly derived risk score in the validation samples was comparable to the performance in derivation study population with Area under the ROC curve ranging from 0.7 to 0.82.

Conclusion Presented in this thesis is the first ever diabetes risk score derived from Africa. It is a simple inexpensive tool for identifying individuals with undiagnosed diabetes in African settings. Further work is needed to externally validate the score in other populations

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Dedication

This thesis is dedicated to my husband and my children

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However much I would like to take credit for the production of this work, it would not have been possible without the enormous contributions from a number of people which made the completion and production of this thesis achievable.

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Abbreviations

ADA	American Diabetes Association
ADDITION	Anglo Danish Dutch Study of Intensive Treatment In peOple with screeN-detected diabetes in primary care study
AIC	Akaike Information Criterion
AUC	Area Under the Curve
BMI	Body Mass Index
BP	Blood Pressure
CI	Confidence Interval
CRIBSA	Cape Town Diabetes Study
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
DPP	Diabetes Prevention Program
ECG	Echocardiography
FPG	Fasting Plasma Glucose
GDP	Gross Domestic Product
GPAQ	Global Physical Activity Questionnaire
HbA1c	Glycated Haemoglobin A 1c
HDL	High Density Lipoprotein
HL	Hosmer Lemeshow

IDF	International Diabetes Federation
IDI	Integrated Discrimination Improvement
IDPP	Indian Diabetes Prevention Program
KZN	Kwazulu Natal
LDL	Low Density Lipoprotein
LMIC	Low and Middle Income Countries
NCD	Non Communicable Diseases
OGTT	Oral Glucose Tolerance Test
RBG	Random Blood Glucose
RCS	Restricted Cubic Splines
ROC	Receiver Operating Characteristic Curve
RPM	Rotterdam Prediction Model
SBP	Systolic Blood Test
SD	Standard Deviation
SE	Standard Error
SES	Socio Economic Status
SSA	Sub Saharan Africa
TC	Total Cholesterol
TG	Triglycerides
US	United States
WHO	World Health Organisation

Chapter 1. Introduction

In most populations a substantial proportion of individuals with diabetes remain undiagnosed (Whiting et al., 2011). There is strong interest in identifying locally practical approaches for identification of those with undiagnosed diabetes. Screening which refers to the application of a test to people who are asymptomatic for the purpose of classifying them with respect to their likelihood of having a particular disease (Hennekens and Buring, 1989) , is a practical approach to identify those with undiagnosed disease so that they can benefit from treatment with the underlying assumption that these will be detected early before the disease progresses to critical stages.

Diabetes care in Tanzania is organized at the secondary and tertiary health care facilities. Diabetes clinics have now been established at all regional hospitals. In Dar es Salaam and the lake zone Region the network extends to the district level. Plans are underway to establish diabetes clinics in all district hospitals throughout the country (Ramaiya, 2005). The health care system comprises of different levels of health care with the lowest level being the dispensary and health centres, which are mainly equipped to provide maternal and child health services. The next level of care is the district hospitals which provide secondary level care and the tertiary level of care are the regional hospitals and the zonal referral hospitals. Access to diabetes care at the community and primary care level is still low; therefore making a diabetes diagnosis at this level is still a challenge therefore presenting a missed opportunity to identify cases that might have benefited from early diagnosis and care.

Diabetes screening is emerging as an important topic in the field of diabetes and has recently received critical attention, with the increasing burden of the disease. A considerable amount of literature has been published on the various screening methods for diabetes, including diabetes risk scores (Echouffo-Tcheugui et al., 2012, Buijsse et al., 2011), and on the importance of using the simple risk scores to increase the yield of screening and promote efficient use of resources (Brown et al., 2012).

However these studies have been mostly conducted in high and middle income countries. So far no study has been published that has looked at aspects of diabetes screening and methods for diabetes screening in the African setting. Most studies looking at diabetes risk scores were conducted in White and Asian populations and the resulting diabetes scores have not been validated in this setting and hence have limited application in Africa (Brown et al., 2012).

The aim of this study is to develop and validate a diabetes risk score suitable for populations in Africa. In particular this thesis focused at developing a risk score that will be applicable across different settings/countries in Africa. Previous studies have demonstrated differences in background characteristics of the study populations contribute to the differences in performance of the risk scores when applied elsewhere. The key question in this thesis is whether the performance of a risk score can be improved by deriving the score with data from multiple countries to create a score that is applicable to other settings.

Thus, in this thesis derivation of a diabetes risk score is described and its internal and external validation are also reported. The study is focused on the derivation and validation of a diabetes risk score to screen for prevalent type 2 diabetes. It is beyond the scope of the study to discuss risk scores for predicting future diabetes and this is therefore excluded in the discussion. It is worth noting that also discussions relating to diabetes are restricted to type 2 diabetes and other types such as diabetes type 1 and gestational diabetes are excluded.

The research data in this thesis are drawn from 2 main sources; data from previous diabetes population surveys in Tanzania, Guinea, Senegal and South Africa and data from a cross sectional survey in Tanzania. The data from the cross sectional study in Tanzania was based on a convenience sample and therefore may not be representative of the Tanzanian population. The sample is likely to include individuals that perceive themselves to be at high risk because individuals received an open invitation to participate.

My main reason for choosing this study is the increasing burden of diabetes in my country as described in Chapter 2 and the lack of diagnostic services for diabetes in the semi urban and rural areas. My conception was that the score would help to identify people at high risk that could be referred to the next level of care for diagnosis and further management.

The overall lay out of the thesis takes the form of nine chapters, including this introductory chapter. The thesis can be divided into three main components which are literature review, derivation of the risk score and lastly validation of the risk score and other existing scores in different populations.

Chapter two begins by laying out background information on diabetes and the burden of diabetes in Africa. Chapter three looks at approaches to diabetes screening and discusses various methods for diabetes screening and their application in the African setting. It lays out the discussions to build the case to support screening of people at high risk of diabetes Vis a Vis the Wilson and Jungner criteria for screening of diseases (Wilson J, 1968). In chapter four existing diabetes risk scores are described and their performances across different populations are explored. The aims and objectives of this research are described in chapter five after outlining the necessary background information for the research. As stated previously, data for the study were obtained from various countries in Africa. Chapter five gives background information on each of the study populations. Data collection methods and a description of how the various variables were assessed are provided. A description of how the background characteristics are likely to affect results of this study is given in this chapter. Chapter five also summarises the characteristics of the different study populations. Chapter six describes the process of deriving and internally validating the new diabetes risk score. In this chapter both the methods undertaken to derive and to internally validate the score, and the results, are described. Since the score was derived from different sources of data meta-analysis results of applying the score in individual data is done to assess heterogeneity and results are presented in chapter six. Chapter seven looks at the validation of the new score in populations independent of the score derivation study populations. The chapter outlines the methods, results and discussion, throughout this chapter the performance of the new score is compared to existing scores based on known measures used to assess diagnostic studies including sensitivity, specificity and measures of discrimination reported as the Area under the Receiver Characteristics Curve (AUC). Chapter eight is concerned with validating the derived score in data from a clinic study in Tanzania. This setting is said to depict the setting in which the score would be used in practice. The utility of the score is discussed in terms of the yield and the number needed to screen at different cut points of the score.

Discussions are found at the end of each chapter as research objectives were described in detail in separate chapters. The last chapter, on page 159, draws up the conclusions and gives a brief summary and critique of the findings and includes a discussion of the implications of the findings to future research in this area.

The term undiagnosed diabetes is used throughout this thesis and is used to define individuals with diabetes who have never been previously diagnosed with the disease and are identified at screening. Also terms “derivation data”, is used to define data from Tanzania, Senegal and Guinea that were used to derive the score and “validation data” is used to define data used to validate the scores which were from South Africa, Guinea and Tanzania.

Chapter 2. Prevalence of Diabetes Mellitus in Africa

2.1 Introduction

The aim of this chapter is to provide background information on diabetes, its definition and the diagnostic criteria. This chapter also includes a detailed account of the prevalence of diabetes in Africa together with a discussion of the associated risk factors. Because of the obvious epidemiological evidence on the differences in diabetes epidemiology among the countries in Sub-Saharan Africa (SSA) and those in North Africa, this review is restricted to those countries within SSA. Other aspects of diabetes epidemiology in the region such as diabetes complications and the economic costs due to diabetes are discussed in Chapter 3 on page 32 . The discussion in this chapter is restricted to type 2 diabetes which is the focus of this thesis.

2.2 Definition and Diagnosis of Diabetes Mellitus

Diabetes Mellitus is a condition that is characterised by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects of insulin secretion, action or both. According to WHO, diabetes is defined as fasting plasma glucose of $\geq$ 7 mmol/l (126mg/dl) or a venous plasma 2h glucose tolerance test of $\geq$11.1 mmol/l (200mg/dl) (WHO, 2006) . Diabetes mellitus can be broadly be categorized into four categories based on the aetiology, these include diabetes type 1 and type 2, gestational diabetes and other specific types. Type 1 diabetes is further classified as auto immune or idiopathic see Figure 2-1. Causes of type 2 diabetes could be insulin deficiency, insulin resistance or both. The other type are the specific types that are as a result of either genetic defects of beta cell function, genetic defects of insulin action, diseases of the pancreas, endocrinopathies, drug or chemical induced diabetes. Other forms diabetes include those that are secondary to infections or are immune mediated (WHO, 2006).

Prediabetes defined as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) is a condition of abnormal glucose metabolism and is associated with an increased risk of diabetes and other cardiovascular diseases (Abdul-Ghani and DeFronzo, 2009, Ford et al., 2010, Færch et al., 2008).

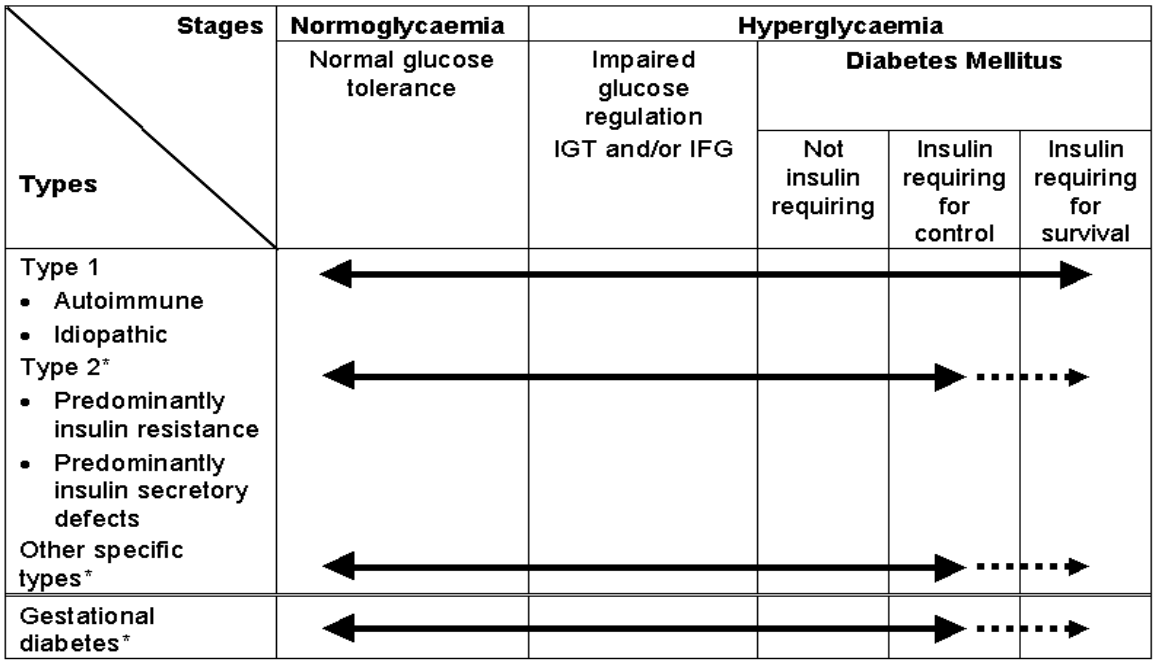

Figure 2-1 Disorders of glycaemia: Aetiological Types and Clinical Stages (WHO, 2006)

Diabetes is associated with serious long term complications that are broadly categorised as micro-vascular: retinopathy, nephropathy and foot complications; and macro-vascular which include cardiovascular complications. Type 2 diabetes mellitus has an insidious onset, and overt symptoms normally manifest/ occur in later stages of the disease. At the time the patients are clinically diagnosed and a number already have complications (WHO, 2006).

The diagnosis of diabetes is based on a threshold value along the glucose range. The cut points for the diagnosis of diabetes are based on plasma glucose levels beyond which the risk of micro vascular complications such as retinopathy increases (Barr et al., 2002) . The diagnostic criteria have been reviewed several times to incorporate new evidence regarding the onset of micro and macro vascular complications along the glucose continuum. The latest diagnostic criteria were published in 1999 where the cut off points for diagnosis of diabetes using fasting glucose were lowered and a concept of impaired fasting glycaemia was introduced (WHO, 2006). In 2011, WHO also endorsed the use of HbA1c for diagnosis of diabetes and recommended a cut-off point of 6.5% (WHO, 2011b) .

Current recommendations for diabetes diagnosis stipulates that diagnosis of diabetes in the absence of clear symptoms should be based on two test (WHO, 2006, ADA, 2013). A single positive test is not diagnostic under such circumstances.

Different tests for the diagnosis of diabetes mellitus will be discussed in detail in Chapter 3 on page 38. Table 2-1 below shows a summary of the current diagnostic criteria for diabetes and impaired glycaemia using fasting blood glucose and 2-hr oral glucose tolerance tests.

Table 2-1 Summary of WHO Diagnostic Criteria for Diabetes and Intermediate Hyperglycaemia

	1965	1980	1985	1999
Normal Fasting glucose 2–h glucose	Not specified <6.1mmol/l	Not defined	Not defined	<6.1mmol/l Not specified but <7.8mmol/l implied
Diabetes Fasting glucose 2–h glucose	Not specified ≥7.2mmol/l	≥8.0mmol/l and / or ≥11.0mmol/l	≥7.8mmol/l or ≥11.1mmol/l	≥7.0mmol/l or ≥11.1mmol/l
IGT Fasting glucose 2–h glucose	Referred to as borderline state 6.1 7.1mmol/l	<8.0mmol/l and ≥8.0 and <11.0 mmol/l	<7.8mmol/l and ≥7.8 and <11.1 mmol/l	<7.0mmol/l and ≥ 7.8 and <11.1mmol/l
IFG Fasting glucose 2–h glucose	Not defined	Not defined	Not defined	≥6.1 and <7.0mmol/l and <7.8mmol/l (if measured)

Values represent venous plasma glucose

2.3 Prevalence of Diabetes and Associated Risk Factors in Africa

2.3.1 Diabetes in Africa, Estimates and Projections

The burden of diabetes is increasing worldwide, with studies reporting higher increase in diabetes prevalence in developing countries (Shaw et al., 2010, Wild et al., 2004, 2009, Whiting et al., 2011, Zimmet et al., 2001). The International Diabetes Federation (IDF) has estimated that 366 million adults (8.3%) had diabetes worldwide in 2011 (Whiting et al., 2011). This estimate by IDF is similar to what has been predicted by the Global Burden of Disease Study Group (Danaei et al., 2011), which in their study estimated that in 2008 there were a total of 347 million adults living with diabetes. The majority of people affected with diabetes reside mainly in low and middle income countries, with China (90.0 millions) and India (61.3 millions) projected to have the largest number of people affected with diabetes in the world (Whiting et al., 2011). In a study from China (Yang et al., 2010) reported that about 92.4 million people had been affected with diabetes and 148.2 million affected with prediabetess (IFG or IGT) signifying a huge burden of disease related to diabetes and prediabetess in this population respectively. The IDF (Whiting et al., 2011) estimates that, by 2030, the number of adults with diabetes is projected to increase by 50.7% and 48% of absolute increase in number of people in diabetes is expected to occur in China and India alone. The largest increase in diabetes is expected in the low income countries with projections of about 93% increase in diabetes prevalence by 2030 compared to 25% increase in higher income countries (Whiting et al., 2011). The rapid increase in diabetes in developing countries is said to be a result of socio economic development that have led to changes in people's lifestyle patterns where people are more likely to be exposed to unhealthy diet and low levels of physical activity in turn which attenuates the individuals' inherent risk of diabetes and other cardiovascular diseases (Zimmet, 1992). Africa is not spared in the growing diabetes epidemic that is more apparent in developing countries. In 2011 the total number of diabetes cases in Africa was estimated to be 14.7 million cases with a total prevalence of 5%, with higher estimates of around 6-8% projected by the Global Burden of Disease Study Group (Danaei et al., 2011) . It is projected that the total number of people with diabetes in Africa will increase by 90% by the year 2030 (Whiting et al., 2011).

2.3.2 Review of diabetes studies in Africa

Search Strategy

The information presented here was obtained by review of key literature on diabetes prevalence and citation tracking from those key publications. Information was also obtained by performing a subject specific search in Medline and Embase, using Ovid software as well as Scopus. A search on diabetes prevalence in Africa yielded a total of 541, 356, and 394 papers in Medline, EMBASE and SCOPUS respectively (Table 2-2). Of these, 503, 335 and 378 papers were excluded at title stage from the above respective databases. At abstract stage, after removing duplicates 29 papers were obtained from the 3 databases using an inclusion criteria outlined in Table 2-3 below. In addition, one paper was found from citation tracking. Excluded studies were those on genetics, studies from other regions other than Africa, studies specifically type 1 diabetes and at abstract stage, those which did not meet the inclusion criteria see Table 2-2.

30 studies on prevalence of diabetes were identified from the search. 5 studies were carried out between 1980 and 1990. Different methods were used to diagnose diabetes and other forms of glucose intolerance. Different criteria were used to define diagnosis: 3, 14 and 12 studies used the 1980, 1985, and 1998/1999 WHO criteria, information on 1 study could not be obtained. Only studies using the current diagnostic criteria for diagnosing diabetes were included in the review. Of the 12 studies identified using the latest criterion for diagnosis, 1 study was excluded due to poor methodology hence 11 studies were included in the review.

Table 2-2 Source of Information for the Literature Search

Method	Sources
Search within clinical databases	MEDLINE, EMBASE, SCOPUS
Cross referencing	Review and original articles
Search within organisation	WHO, IDF, UK Diabetes Association, American Diabetes Association, Tanzania Diabetes Association,

Table 2-3 Search Strategy Results for Studies on Prevalence of Diabetes in Africa

MEDLINE (Search Dates: 1980-2010)	
Search history	**Results**
1. Diabetes mellitus.mp. or diabetes mellitus	191122
2. Prevalence.mp. or prevalence	289714
3. Exp Africa/ or Africa$.mp.	187809
4. 1 and 2 and 3	1078
5. limit 4 to (human and (adult <18 to 64 years> or aged <65+ years>)	1077
6. Population.mp. or population	660022
7. 5 and 6	541
8. From 7 keep 26, 48, 60, 101, 104, 113...	38
EMBASE(Search Dates: 1980-2010)	
1. Diabetes mellitus.mp. or diabetes mellitus	255284
2. Prevalence.mp. or prevalence	281811
3. Exp Africa/ or Africa$.mp.	125035
4. 1 and 2 and 3	1154
5. limit 4 to (human and (adult <18 to 64 years> or aged <65+ years>)	732
6. Population.mp. or population	585320
7. 5 and 6	356
8. From 7 keep 26, 48, 60, 101, 104, 113...	21
SCOPUS	
1. TITLE-ABS-KEY(**diabetes mellitus** AND **Africa** AND **prevalence**) AND PUBYEAR AFT **1979** AND (LIMIT-TO(SUBJAREA, "**MEDI**") OR LIMIT-TO(SUBJAREA, "**MULT**"))	394
2. From 1 keep	16

Table 2-4 Inclusion Criteria for Studies on Diabetes Epidemiology in Africa

Criteria	**Description**
Population	- Studies on burden of diabetes - Studies that are specific to Africa
Intervention	- Diabetes defined using 1998 WHO criteria
Outcome	- Prevalence
Study design	- Cross sectional

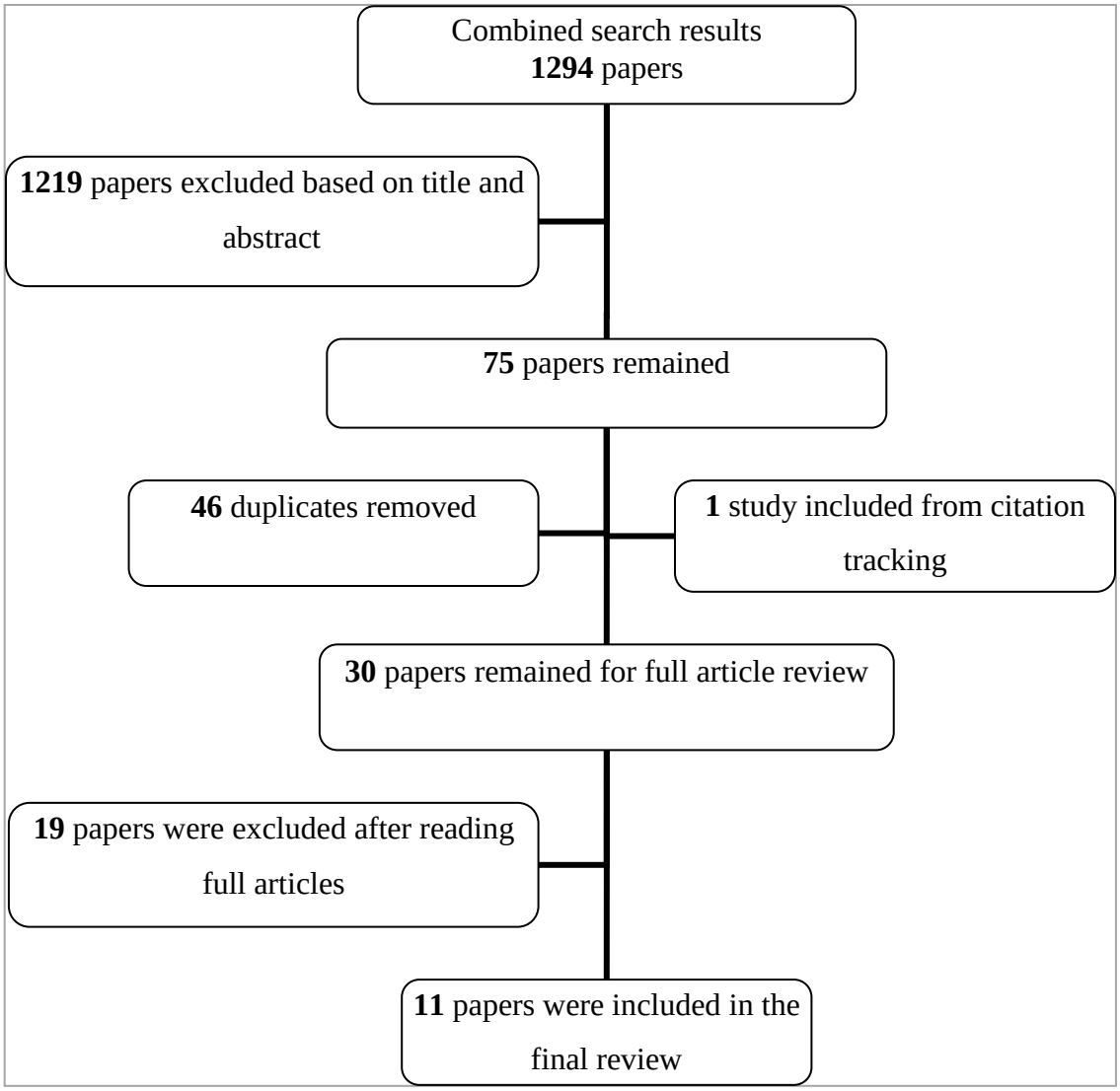

Figure 2-2 Consort Diagram of Summarizing the Selection of Papers Included in the Review of Diabetes Prevalence Studies in Africa

Results

A review of studies on diabetes prevalence in Africa published within the last decade using the 1998 WHO criteria for diagnosing diabetes, shows varying prevalence across countries, the results of which are shown in table 2-5 below. From the search strategy, the identified studies are from 7 Sub-Saharan countries namely Nigeria (Nyenwe et al., 2003, Okesina et al., 1999, Oladapo et al., 2010), South Africa (Erasmus et al., 2001, Alberts et al., 2005, Motala et al., 2008), Tanzania (Aspray et al., 2000), Cameroon (Sobngwi et al., 2002), Ghana (Amoah et al., 2002), Guinea (Balde et al., 2007) and Kenya(Christensen et al., 2009) . In these studies the diagnosis of diabetes was made either using Oral Glucose Tolerance Test (OGTT) (Amoah et al., 2002, Balde et al., 2007, Erasmus et al., 2001, Motala et al., 2008, Nyenwe et al., 2003, Christensen et al., 2009) or fasting glucose (Aspray et al., 2000, Oladapo et al., 2010, Sobngwi et al., 2002).

Table 2-5 Prevalence of Diabetes in Sub-Saharan Africa

Country	(Author, Year)	(Rural/Urban)	Sample Size			Response rate %	Age	Diagnosis	Prevalence Diabetes [% (95%CI)]				Undiagnosed diabetes
			M	F	T				M	F	T	R&U	
Nigeria	(Okesina et al., 1999)	Rural	278	222	500	-	>40	FPG	-	-	*2.6	-	-
	(Nyenwe et al., 2003)	Urban	273	229	502	67	>40	WHO 1999 OGTT	*7.7(4.6-10.8) , 9.1	*5.7(2.7-8.7), 6.3	*6.8 (4.6-9.0), 7.9	-	41.2%
	(Oladapo et al., 2010)	Rural			2000		18-64	FBG	2.1	2.8	2.5		27.0%
South Africa	(Erasmus et al., 2001)	Urban	-	-	374	-	>20	WHO 1998 OGTT	-	-	4.5(1.54-7.42	-	-
	(Alberts et al., 2005)	Rural	498	1608	2016	-	>30	WHO 1999 FPG	*8.5	*8.8	-	-	-
	(Motala et al., 2008)	Rural	210	815	1025	78.9	>15	WHO 1998 OGTT	3.5	3.9	3.9	-	85.0%
Tanzania	(Aspray et al., 2000)	Urban	332	438	770	80-85	>15	WHO 1998 & ADA	5.9	5.7	-	-	79.0%
		Rural	401	527	928	65-82		FPG	1.7	1.1	-	-	92.0%

Country	(Author, Year)	(Rural/Urban)	Sample Size			Response rate %	Age	Diagnosis	Prevalence Diabetes [% (95%CI)]				Undiagnosed diabetes
			M	F	T				M	F	T	R&U	
Cameroon	(Sobngwi et al., 2002)	Urban	525	658	1183	-	>15	WHO 1998 FPG	6.2 (3.7-8.9)	4.7(2.6-6.8)	-	-	-
		Rural	523	759	1282	-			4.7 (2.5-6.9)	2.9(1.5-4.4)	-	-	-
Ghana	(Amoah et al., 2002)	Urban	1860	2873	4733	75	>25	WHO 1998 OGTT	-	-	6.1	-	69.7%
Guinea	(Balde et al., 2007)	Urban	371	515	886	-	>35	WHO 1998 OGTT	-	-	*7.7 (5.9-9.4)	6.7 (5.5-7.9)	59.0%
		Rural	359	292	651	-			-	-	*4 (2.5-5.5)		100.0%
Kenya	(Christensen et al., 2009)	Urban	-	-	281	98.2	>17	WHO 1999 FBG & OGTT	-	-	12.2(5.4-23.2)	4.2(2.0-7.7)	21.0%
		Rural	-	-	1178				-	-	2.2(0.8-5.2)		48.0%

Key

**Crude Prevalence Rates, M= Male, F= Female, T=Total (Both males and Females), R&U= Rural and Urban*

Nyenwe (2003) presents data for both crude and standardised prevalences

The prevalence of diabetes in Sub-Saharan countries ranged from less than 2% in rural Tanzania (Aspray et al., 2000) to 12.2 in urban Kenya (Christensen et al., 2009) which is the highest reported prevalence in sub-Saharan Africa see table 2-5 above. The findings of diabetes prevalence across countries were marked with clear urban rural differences, with a higher prevalence being reported in urban areas (Figure 2-3).

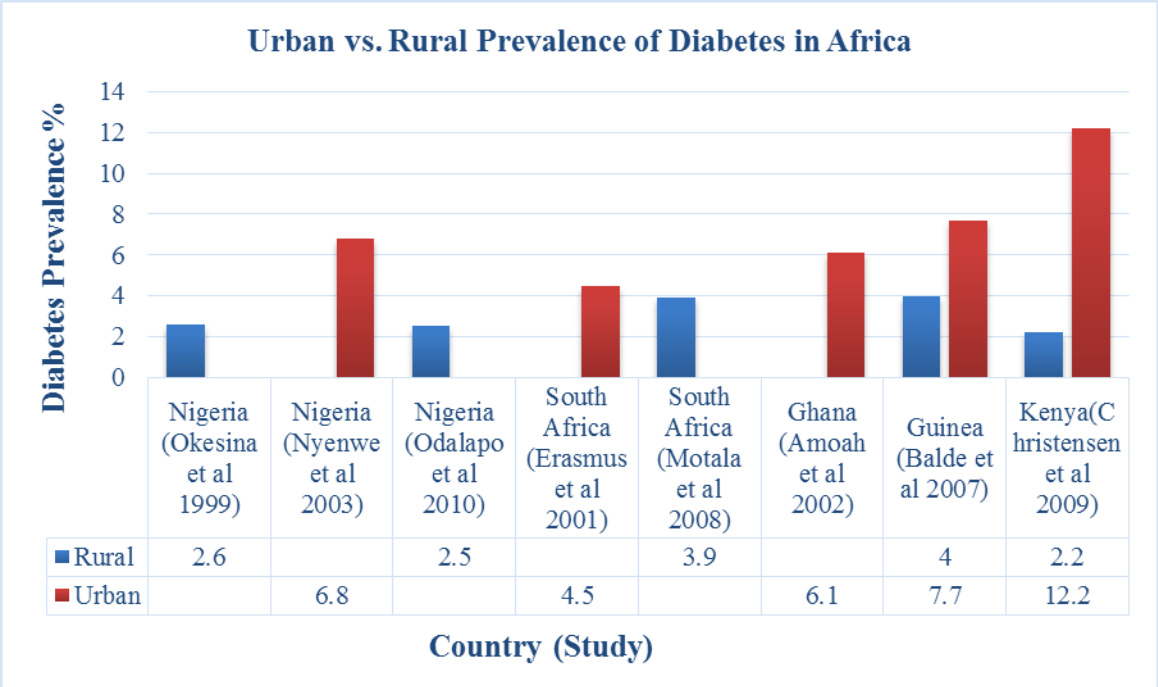

Figure 2-3 Urban Vs. Rural Prevalence of Diabetes in Africa

Nigeria, Tanzania and Kenya reported a rural prevalence of diabetes of <3% (Aspray et al., 2000, Christensen et al., 2009, Okesina et al., 1999, Oladapo et al., 2010), however, higher prevalence of diabetes is reported in rural areas such as those reported in rural South Africa, Cameroon and Guinea (Alberts et al., 2005, Balde et al., 2007, Motala et al., 2008, Sobngwi et al., 2002) with rural diabetes prevalence ranging from 3.9% to 8.8%.

The variation in prevalence between countries could partly be explained by the method used for diagnosis (Barr et al., 2002), OGTT tends to identify more cases that would otherwise be missed if Fasting Glucose alone is used for diagnosis. A study (Kim et al., 2008) showed that compared to OGTT, Fasting Glucose measurement identified only about 56% of the cases. A study in Africa also reported that there would be 36% less diabetes cases if fasting alone was used for diagnosis (Motala et al., 2008) .

The differences in the prevalence of diabetes between countries could also be due to the variances in structure of the sampled population such as age, degree of urbanisation, sex and other risk factors associated with diabetes. Also sample size, sampling methods and the response rates could have biased the results in some studies.

All the studies were population based studies with random selection of participants; however the study in Kenya (Christensen et al., 2009) included a convenient sample for the urban population also the sample size seem to be small to estimate prevalence in this population with good precision as evidenced by the large confidence intervals (urban prevalence 12%, 95% CI 5.4% to 23.2%). Similarly none of the studies took into account the different categories they used in analysing their data e.g. sex and urban vs. rural in their sample size calculations, which may introduce bias to the overall estimates.

Also, studies that reported enrolling participants above the age of 30 yrs. described higher prevalence of diabetes in general, especially since some of the studies report only crude prevalence rates (Table 2-5). Level of urbanisation among the study areas could also impact on the results of the studies; this cannot be thoroughly assessed in the present studies as there are no formal indicators of urbanisation presented in majority of the studies, as discussed in detail in section below.

2.3.3 Associated Risk Factors for Type 2 Diabetes

The variations in prevalence of diabetes between countries and between rural and urban settings could be explained by differences levels of risk factors such as socio economic status , the degree of urbanization and the background characteristics such as age, sex, ethnicity, diet and the levels of physical activity as mentioned above (Assah et al., 2011, Boyle et al., 2001). Risk factors for diabetes can be grouped into modifiable and non modifiable risk factors, these various risk factors for diabetes and their implications on diabetes prevalence in Africa are further discussed in subsequent paragraphs.

Modifiable Risk Factors

Physical inactivity is one of the modifiable risk factors for diabetes. Previous studies have demonstrated that physical activity reduces overall risk of developing diabetes and improves cardio-metabolic risk profile (Manson et al., 1991, Helmrich et al., 1991, Hu et al., 2004), the mechanism of which is linked to increased secretion and insulin sensitivity as well as

increased fat metabolism (Mayer-Davis et al., 1998) whose overall effect is reduction in the risk of diabetes. Available literature on the relationship between levels of physical activity and diabetes from Africa suggest an inverse relationship (individuals with high levels of physical activity had lower risk of diabetes) between physical activity and diabetes however these studies have been largely cross sectional and have used different methods to define and measure physical activity (Aspray et al., 2000, Sobngwi et al., 2002) such as the Global Physical Activity Questionnaire (GPAQ), and the Sub Saharan Africa Physical Activity Questionnaire. Overall the studies have demonstrated lower levels of physical activity in urban compared to the rural settings (Aspray et al., 2000, Sobngwi et al., 2002, Jamison et al., 2006) . The physical activity questionnaires are subject to bias and their application vary widely across settings as a result contrary to expectations some of these studies did not show statistically significant results in diabetes risk reduction with increased physical activity levels (Sobngwi et al., 2002). Other studies on physical activity in Africa conducted in Cameroon using more objective measures of physical activity showed a clear reduction in cardio metabolic risk factors including blood glucose with increased physical activity levels (Mensah, 2008, Jamison et al., 2006).

The association between diabetes and overweight and obesity is a widely known concept in the literature. A study in the US (Narayan et al., 2007) showed that the lifetime risk of diabetes at 18 years increased from less than 10% to more than 70% in both males and female for individuals with normal BMI to individuals with BMI of more than 30kg/m^2. The main limitation of this study was that diabetes and obesity status were based on self-reports but results clearly underscore the role of obesity in increasing overall risk of diabetes.

Several studies on diabetes prevalence from Africa have attempted to describe the relationship between diabetes and measures of obesity defined as BMI, Waist Circumference, Waist Hip Ratio and Hip Circumference. In these studies results showed that the persons diagnosed with diabetes had higher mean values of BMI, waist circumference or waist hip ratios depending on the methods used for assessing obesity in the study (Amoah et al., 2002, Aspray et al., 2000, Balde et al., 2007, Christensen et al., 2009, Motala et al., 2008, Nyenwe et al., 2003) . The relationship between BMI and diabetes varied across research settings, where some studies reported BMI to have a stronger association with diabetes among males (Aspray et al., 2000, Christensen et al., 2009) , in some studies the association of BMI and

diabetes did not reach statistical significance (Balde et al., 2007, Nyenwe et al., 2003). The observed differences could be explained by the fact that Africans tend have less visceral fat for a given Waist Circumference and BMI compared to Whites and therefore universal cut off points used may not confer similar risk in different ethnicities (Caroll et al. 2008, Camhi et al. 2011).

Waist hip ratio as an independent predictor of diabetes showed statistically significant association in studies from South Africa, Guinea and Nigeria (Balde et al., 2007, Motala et al., 2008, Nyenwe et al., 2003) , but a weaker association was reported in a study from Tanzania (Aspray et al., 2000). Christensen et al (2009) (Christensen et al., 2009) compared the relation of waist hip ratio by sex and reported a stronger association among males compared to females. A study in Guinea (Balde et al., 2007) which compared the association of waist hip ratio and waist circumference in relation to the risk of diabetes reported that, waist circumference showed a stronger association than waist hip ratio. Hip circumference as a measure of central obesity was reported only in one study (Motala et al., 2008) and findings demonstrated an inverse relationship between hip circumference and diabetes.

Non Modifiable Risk Factors

The prevalence of diabetes is reported to vary across age groups, the different age groups with significantly increasing prevalence with increasing age. For example a study in Ghana (Amoah et al., 2002) found that the prevalence of diabetes was almost six times in the older age category . Increased prevalence of diabetes in older age groups is also reported in a study of diabetes in a rural population in South Africa (Motala et al., 2008) and in Nigeria (Nyenwe et al., 2003). This could be explained by the changes in population structures with improving life expectancy where more adults are now surviving into older age exposing them to such degenerative diseases. For example in Tanzania although children and young adults form the majority of the population; where almost half the population is below 15years, the proportion of those aged 65 years and above has been increasing steadily over the last 2 decades (UN, 2010), according to the National Bureau of statistics the population of those aged 65 yrs. and above in Tanzania was estimated to be 717,098, 981,839 and 1,347,085 in 1978, 1988 and 2002 respectively. In 2002 the proportion of the population aged 65 and above was estimated to be 3.9% (The United Republic of Tanzania Population and Housing Censuses of 1978, 1988 and 2002)

On comparing the mean age of the study populations age distribution having lower mean age does not confer lower prevalence of diabetes. For example the urban population surveyed in the Tanzania (Aspray et al., 2000) had a mean age of about 30 years, but with a relatively higher prevalence of diabetes compared to the rural population which were older but with lower overall prevalence of diabetes. Similarly the study in Kenya (Christensen et al., 2009) had one of the highest diabetes prevalence but relatively low mean age of study participants compared with other studies from Sub-Saharan Africa . These findings indicate that the lifestyle factors are more important than aging process alone in the aetiology of diabetes.

There is variation in the findings reported from studies on the association of diabetes and sex across different study populations. There is little information on relationship between sex and diabetes in Africa however results from diabetes studies in different countries in Africa report higher prevalence of diabetes in males (Aspray et al., 2000, Nyenwe et al., 2003, Sobngwi et al., 2002) and others (Alberts et al., 2005, Motala et al., 2008, Oladapo et al., 2010) report higher diabetes prevalence among the female respondents unlike in Whites where male sex is always associated with higher risk of developing diabetes. The observed differences in the prevalence of diabetes between males and females seem to correlate with the overall distribution of the risk factors in that particular study population, studies with higher levels of risk factors such as obesity, smoking, older age etc in men compared to women had higher prevalence of diabetes and the reverse is true . Also gender is confounded with lifestyle for example, a higher proportion of men smoke and tend to have higher central obesity than women.

Differences in the overall risk of diabetes between males and females need further consideration as there is no conclusive evidence on the relationship between diabetes and sex in this setting as the current studies have not been able to answer this important question. Results from studies in Africa provide inconclusive results over the overall risk of diabetes among males and females as the studies themselves are prone to bias due to small sample size and male or female predominance in the sampled population (Alberts et al., 2005, Amoah et al., 2002, Motala et al., 2008). For example the study by Motala had >70% females (Motala et al.2008).

As mentioned previously findings from the current (this chapter) study and studies of diabetes prevalence in Africa are characterized by a clear urban rural differences with higher burden of diabetes in the urban areas (Mbanya et al., 2010, Motala et al., 2008). Drawing upon these findings there is evidence to suggest influence of urbanization on the risk of developing diabetes. The extent to which urbanization relates to the risk of diabetes has been reported in a few studies in Africa measured as current urban residence or duration of stay in an urban environment (Aspray et al., 2000, Motala et al., 2008, Sobngwi et al., 2002). These measures are hardly generalizable as there is no uniform definition of urbanization in these studies .The duration of exposure to an urban environment also relates to age of the individual which needs to be considered when assessing the association between urbanization and diabetes risk. Despite these drawbacks, findings from studies seem to support the present hypothesis. A study in Tanzania showed that living in the urban area increased the odds of diabetes by five to six fold (Aspray et al., 2000), urban residency was also associated with an increased risk of diabetes of up to 3.7 times in a study from Kenya (Christensen et al., 2009) . In addition a study from South Africa reported a positive significant relationship between the prevalence of diabetes and the proportion of time people spent in an urban environment, in this particular study urbanization is defined as >40% of life spent in the city (Motala et al., 2008). Other studies for example from Tanzania and Cameroon urbanization was defined as living in an urban area regardless of the time spent in that area (Aspray et al. 2000, Assah et al.2011). These findings call for standardization of indicators so that risk factors can be assessed uniformly and more objectively across settings.

A longitudinal study on the effects of urbanization was reported by Unwin et al (Unwin et al., 2010), where they measured behavioral and biological risk factors for diabetes and other non-communicable diseases among individuals before they moved to urban areas and followed them up a year later found that there were significant increase in their levels of cardio-metabolic risk profile after they had lived in the urban area. Similar findings are also reported in a review of effects of urbanization on metabolic risk factors by Hernandez and colleagues (Hernández et al., 2012).The possible explanation on the association between urbanization and increased risk of diabetes is increased exposure to environmental factors that promote poor dietary patterns and low levels of physical activity in urban areas (Gong et al., 2012).

Family history of diabetes is also an independent risk factor for diabetes (Valdez et al., 2007). It has been shown previously that a person with a family history of diabetes is two to six times more likely to have diabetes compared to an individual without family history of diabetes and the strength of the association relates to the number of family members affected (Harrison et al., 2003). Some studies of diabetes prevalence in Africa explored the association between family history of diabetes and the risk of diabetes. The strength of the association ranged from a non-significant weak association in Kenya (OR 1.12, 95% CI 0.57 to 2.85) (Christensen et al., 2009) to strong association in Nigeria (OR 9.45, 95% CI 3.49 to 35.54) (Nyenwe et al., 2003). With regard to ethnicity a few studies have looked at the prevalence of diabetes in different ethnic groups these include studies from Kenya and Nigeria. These studies have demonstrated a clear difference in the risk of diabetes in the different ethnic groups. A study in Kenya has demonstrated a higher risk of diabetes among the Luo ethnic groups compared to the Kamba and Maasai (Christensen et al., 2009). In West Africa higher prevalence of diabetes has been reported among the Fulani ethnic groups (Balde et al., 2007, Nyenwe et al., 2003). Ethnic differences could probably explain the observed differences in diabetes prevalence across countries.

Social economic status has also been found to be associated with diabetes in previous studies (Kumari et al., 2004, Timothy et al., 2011) ; in these studies individuals of higher socioeconomic status had lower risk of diabetes however in this review no study was found describing the relationship between diabetes and different levels of income. Income levels tend to modify the exposure to the different modifiable risk factors.

2.4 Undiagnosed Diabetes in Africa

In the previous section the prevalence of diabetes and the contributing risk factors were discussed and there is evidence that diabetes is no longer the disease of the rich and is prevalent even in rural areas. One of the challenges identified in these studies is the high prevalence of undiagnosed diabetes. In the identified studies the prevalence of undiagnosed diabetes was high with prevalence of undiagnosed diabetes ranging from 21% in urban Kenya (Christensen et al., 2009) to 100% in rural Guinea (Balde et al., 2007) . The prevalence of undiagnosed diabetes was generally higher in rural than urban areas for example in Guinea the prevalence of undiagnosed diabetes was 59% in urban Guinea whilst

all (100%) individuals in the rural area were diagnosed at screening (Balde et al., 2007), Similarly studies in Kenya and Tanzania showed a similar pattern (Aspray et al., 2000, Christensen et al., 2009) . The high prevalence of undiagnosed diabetes in the African setting is a reflection of the poor access to health facilities and also lack of diagnostic capacity at the available health care facilities which is more evident in rural compared to urban areas.

2.5 Discussion

The aim of this chapter was to provide background information on burden of diabetes and to review the prevalence of diabetes in African countries.

The global burden of diabetes has increased compared to what had been previously predicted as described by the recent studies (Danaei et al., 2011, Whiting et al., 2011). Previous studies had underestimated the true burden of diabetes in their projections (Shaw et al., 2010, Wild et al., 2004). In their study, Shaw et al predicted that there will be 285 million people living with diabetes in 2010, however current data show that there over 300 million people living with diabetes. The differences could be due to availability of more data emanating from recent diabetes studies showing a true increase or due to differences in methodology and the type and number of studies included from the different countries.

These studies provide the projections of diabetes burden but do come with a few limitations which affect the precision of their estimates including lack of accurate data. For example most of the data used in these studies to make projections come from studies that are not nationally representative, in the Global Burden of Disease Study only 29% of the studies used came from national surveys, about 46% of all countries included in the analysis had no country data, the data used was extrapolated from studies in neighbouring countries (Danaei et al., 2011).

This chapter also included a review of diabetes studies from Africa. The review was restricted to studies using the 1999 diagnostic criteria for diabetes (2006). This review has shown that diabetes is prevalent in both urban and rural areas of sub-Saharan Africa, with the highest rates of diabetes (12.2%, 95% CI 5.4% to 23.2%) reported in Kenya (Christensen et al., 2009). Compared to previous studies diabetes seems to have increased in different parts of Africa. For example, in Nigeria compared to previous studies (Erasmus et al., 1989, Owoaje et al., 1997, Olatunbosun et al., 1998)., prevalence of diabetes has increased two to

three fold compared to results from recent surveys; from less than 2% in 1989 (Erasmus et al., 1989) to more than 6% in 2003 (Nyenwe et al., 2003). Similarly, the same trend is observed in Cameroon, Tanzania and South Africa where the studies showed an incremental increase in the prevalence of diabetes in subsequent studies compared to previous studies (Ahren and Corrigan, 1984, Aspray et al., 2000, Erasmus et al., 1989, Mbanya et al., 1997, McLarty et al., 1989, Omar et al., 1985, Omar et al., 1993, Sobngwi et al., 2002).

With the exception of the high prevalence of diabetes reported from Kenya (Christensen et al., 2009), the prevalence of diabetes found in this review is lower than what has been reported previously in other African countries where studies reported high prevalence of diabetes, such as in Mauritius (13%-18%) (Söderberg et al., 2005, Söderberg et al., 2004), Seychelles (11%) (Faeh et al., 2007), Tunisia (9.3%) (Gharbi et al., 2002), Northern Sudan (8.3) (Elbagir et al., 1998) and Egypt (9.3%) (Herman et al., 1995). These differences in diabetes prevalence might be due to genetic susceptibility and also environmental factors such as lack of physical activity and unhealthy diet. Previous studies have reported higher prevalence of diabetes in individuals of Arab and Asian origin, with IDF estimates showing that countries in North Africa and the Middle East have the highest prevalence of diabetes (Whiting et al., 2011). Similarly, studies in Sub Saharan Africa (SSA) have shown higher prevalence of diabetes among individuals of Asian Origin compared to native Africans, for example in Tanzania the prevalence of diabetes in this ethnic group was 9.1% (Ramaiya et al., 1991) higher than what is reported in the general population. Higher diabetes prevalence has also been reported within the native Africa ethnic groups such as the Fulani in West Africa (Balde et al., 2007, Nyenwe et al., 2003) and among the Luo in Kenya (Christensen et al., 2009), but these studies could not explain the reasons for the observed differences. Therefore, more research is needed in this area to explain these unanswered questions. These studies clearly show that diabetes is no longer just a disease of western countries.

Urbanization and sedentary lifestyle has been pointed out as a major factor for the rise of diabetes cases and its associated risk factors in developing countries. Diabetes prevalence in Africa has been characterized by urban rural differences, as shown in this review, whereby there is tendency towards higher prevalence in urban areas but with rapid urbanization of rural areas there is loss in the urban rural gradient in the prevalence of diabetes in Africa. As has been reported in this review, studies are now reporting high prevalence of diabetes in the

rural areas when compared to what was reported in older studies (Motala et al., 2008, Sobngwi et al., 2002).

The prevalence of diabetes in Africa seems to peak at a somewhat younger age compared to what has been reported from developed countries (Whiting et al., 2011). In this review the prevalence of diabetes escalates after the age of 40 and in most studies reaches a maximum in the 50 – 60 years age band (Amoah et al., 2002) whilst in developed countries the peak age is above 60, and in others > 70 years age group . This could explained by the population structure where the majority of the population are in the younger age groups for example in developed countries the like Sweden, United Kingdom, USA and Japan the population of those aged 60 years and above was 39.5%, 36%, 29.2% and 40.7% respectively, compared to only 11.6%, 9.6%, 9.5% and 7.1% in South Africa, Tanzania, Malawi and Nigeria respectively (United Nations Demographic Year Book, 2001).

Obesity has been found to be a risk factor for diabetes, a finding which is consistent with what is widely known in the literature; however there is no conclusive evidence on the utility of the various anthropometric measures such as BMI, waist circumference and waist hip ratio. The lack of consistent significant association between these measures and diabetes found in this review could be due to the lack of appropriate cut off points that define risk in this population. For example, a study in China showed that the appropriate cut off points varied across sex categories and they were below the universally recommended cut points for both BMI and waist circumference (Xu et al., 2010). Qing and Nyamdori (Qiao and Nyamdorj, 2010) also found in their study that there were no universal cut points for anthropometric measures and that generally Whites had higher cut off points for the anthropometric measures compared to populations of Asian origin. Therefore, there is a need for further studies in this area in Africa to derive appropriate threshold values to define diabetes in this population.

Studies in this review have also demonstrated an association between physical activity and the risk of type 2 diabetes. The association is weaker than what has been reported elsewhere but this could be explained by the more subjective methods employed to measure levels of physical activities in these studies and this area deserves further consideration. There is need to improve and validate the existing methods with more objective measures, and design

studies to explore issues that may affect levels of physical activity and their assessment in this setting which is culturally diverse.

Data on the effects of economic status on diabetes from the reviewed studies are scarce Herman and colleagues. (Herman et al., 1995) studied the association of socio economic status (SES) and diabetes in Egypt and they report higher levels of diabetes, sedentary lifestyle and obesity among people of higher SES. For example, in their study Herman and colleague reported a prevalence of diabetes of 13.5 % among persons of low SES versus 20% among those in with high SES contrary to what is reported from developed countries where people of low socioeconomic status are at more risk of diabetes (Kumari et al., 2004, Connolly et al., 2000). In Africa, this could be explained by increased exposure to a western way of living in those with higher economic status than their counterpart and also higher levels of obesity, rather than SES being an independent risk.

The reason for lack of data on SES in studies from SSA could be due to lack of uniformly applicable methods of assessment as SES is defined in different ways including income levels, possession of household amenities, occupation/working status or level of education, having electricity and electrical items, type of roofing etc. These indicators are especially difficult to measure in African settings where the majority of people do not have formal education, or employment and also it may be difficult to express their wealth in terms that can be consistently assessed across settings. Other measures of economic status such as; housing tenure; car ownership may not be applicable in many settings, especially in rural areas. Classification of income levels also depends on the general wealth of the population and therefore differs across settings. Income level also changes over time and is influenced by family size. Studies have demonstrated that even Africans are at risk and show higher prevalence of diabetes when they move abroad compared to individuals with similar ethnic backgrounds, with the improvement in SES and increased exposure to western lifestyle, the burden of diabetes in Africa is likely to increase at an alarming rate.

It is clear that diabetes is increasing in Africa and some of the risk factors for diabetes are modifiable. If the current trends continue the burden of diabetes will be unbearable with economic, health and social consequences. There is a need to strengthen the health care system in these countries to respond to these emerging conditions with strategies along the

whole continuum from primary, secondary to tertiary prevention. There is need to put in place mechanisms to identify high risk individuals so that they can receive appropriate care. Given the high rates of undiagnosed diabetes screening could be a feasible approach to identifying those that need prevention and treatment interventions. The next chapter will discuss issues related to diabetes screening and the different strategies to identify individuals at high risk of diabetes and the existing opportunities for primary and secondary prevention of type 2 diabetes.

Chapter 3. Diabetes Screening

3.1 Introduction

As the previous chapter illustrated, the burden of diabetes is increasing worldwide. The prevalence of undiagnosed diabetes is also high especially in low income countries where people have poor access to health care. Studies have shown that diabetes and diabetes related complications can be reduced by lifestyle or pharmacological interventions. A review of available evidence has shown that diabetes screening could be worthwhile (Engelgau et al., 2000, Echouffo-Tcheugui et al., 2011, Simmons et al., 2010, Waugh et al., 2007); however there is a lack of literature regarding the evidence for diabetes screening with application to African settings. This chapter therefore looks at the available evidence on diabetes screening vis-à-vis the criteria for screening for diseases in the African context.

3.2 Definition of Screening

'Screening is the process of identifying those individuals who are at sufficiently high risk of a specific disorder to warrant further investigation or direct action' (Wilson J, 1968). Three approaches to screening will be considered, these include; screening the entire population (mass screening), selective (targeted) screening which is applied to subjects being identified at high risk, and opportunistic screening, where screening is offered to subjects who attend to health care professionals for a reason other than the disorder targeted for screening (WHO, 2003).

3.3 Criteria for Screening of Diseases versus Diabetes Screening

For a disease to be recommended for screening, several conditions, proposed by Wilson and Jungner (Wilson J, 1968) must be met (see text box)

1. The disease should be an important health problem
2. There should be an accepted treatment for patients with recognised disease
3. Facilities for diagnosis and treatment should be available
4. There should be a recognisable latent or early asymptomatic stage
5. There should be a suitable test or examination and should be acceptable to the population
6. The natural history of the condition including development from latent to overt stages of the disease should be adequately understood
7. There should be a clear policy whom to treat as patients
8. The cost of case finding including diagnosis and treatment of patients diagnosed should be economically balanced in relation to possible expenditures on medical care as a whole
9. Case finding should be an on-going process

Wilson and Jungner Criteria for Screening of Diseases

Below is the critical review of the available evidence on each of the criteria in relation to diabetes screening

3.3.1 Is Diabetes an Important Health Problem in Africa?

Emerging evidence shows that diabetes is an increasing problem especially in low and middle income countries such as countries in Africa (Whiting et al., 2011). Diabetes is associated with a substantial burden of premature morbidity and mortality. Studies from White populations have shown that the risk of death among people with diabetes is about two fold that of individuals without diabetes (Chiasson et al., 1998, Barr et al., 2007), with a global estimate of excess deaths attributable to diabetes of 6.8% in 2009 (Roglic and Unwin, 2010). It is estimated that in Africa 280,000 deaths are attributable to diabetes accounting for 6.1% of all deaths among those age 20-79 years also, diabetes is an important cause of premature mortality in the region (2012, Roglic and Unwin, 2010). Diabetes mortality in Africa is probably underestimated given the high proportion of people with undiagnosed diabetes and also diabetes is infrequently recorded as a cause of death, because the tendency is towards recording the immediate cause of death and not the underlying conditions (Roglic and Unwin, 2010).

Diabetes is also known to increase the risk of macro vascular disease by 2 to 4 fold (WHO, 2011a, WHO, 2007) and is related to high rates of microvascular complications (end-stage renal disease (Herman et al., 2005), visual impairment (Saaddine et al., 2006), and peripheral neuropathy (Narayan et al., 2007).

Diabetes also puts a strain on health care systems of these poor resource countries, in 2010 it was estimated that the cost of diabetes care in Africa was about 7% of total health expenditure (Zhang et al., 2010). IDF estimates that a total of 2.8 billion USD was spent on diabetes care in Africa in 2011, and is expected to rise by 61% in 2030 (Ali et al., 2012). A study in Tanzania estimated that the cost of diabetes care for the year 1989/1990 was 287 USD and103 USD for patients requiring insulin and those not requiring insulin respectively in a population with gross capital income ranging between 160 to 200 USD, creating a huge burden to the government, the patients and their families (ADA, 2013). Kirigia et al 2009 also estimated that in the year 2000 countries in Africa incurred a total economic loss of about USD 25.5 billion due to diabetes (Kirigia et al., 2009) . The cost estimates would probably be higher if disease-related medical costs for the extremely high proportion of people with undiagnosed diabetes were recognized and accounted for, also indirect costs

from lost productivity due to disability, premature mortality and absenteeism can be staggering (ADA, 2013, Barcelo et al., 2003, Kirigia et al., 2009).

3.3.2 Is the Natural History of Diabetes Adequately Understood?

The natural history of type 2 diabetes is relatively well understood and includes an asymptomatic phase comprised of prediabetess with an estimated average duration of 8.5 to 10.3 years (Bertram and Vos, 2010), and preclinical latent diabetes stage that could last for about 9 to 12 years (Harris et al., 1992). In various populations, prediabetess states are less likely to regress to normoglycaemia, and are associated with a high risk of progression to overt type 2 diabetes, with an annualized relative risk of 4.7-12 % and absolute annual risks of 5-10% (Gerstein et al., 2007). The progression rate may be particularly high in populations like South Asians where annual progression rates as high as 18.5% have been reported (Ramachandran et al., 2006). Higher rates of conversion from prediabetess to diabetes are described in persons with impaired glucose tolerance and both impaired glucose tolerance and impaired fasting glucose (Rasmussen et al., 2007, Gerstein et al., 2007, Meigs et al., 2003, Qiao et al., 2003, Rasmussen et al., 2008, Gao et al., 2010)

Initial stages of diabetes are subclinical and by the time patients start experiencing symptoms complications may have occurred. Studies mostly in Whites with newly diagnosed diabetes, either conventionally or through screen-detection, have revealed the presence of chronic diabetes complications in up to 50% of cases at the time of diagnosis (Echouffo-Tcheugui et al., 2011, Spijkerman et al., 2003, Herman et al., 1998). Given the susceptibility of some populations of developing countries (e.g., South Asians) to diabetes-related complications and their high progression rate (Ramachandran et al., 2006), the prevalence of complications among screen-detected patients from these groups is likely higher than that observed among Whites. There is limited information on the prevalence of complications among new diabetes patients in Africa but a study in Uganda reported that at the time of diagnosis patients had both macro and micro vascular complications, with 46% having neuropathy and about 28% reporting having poor vision (Nambuya et al., 1996). The prevalence of complications among new patients is likely to be higher at presentation because of poor access to care and hence patients are likely to be diagnosed at a later stage of the disease.

3.3.3 Is There Accepted Treatment for Patients with Recognized Disease?

Interventions for Undiagnosed Diabetes

There is no direct evidence from randomized trials on the benefit of early detection of diabetes from Africa but the Anglo Danish Dutch Study of Intensive Treatment In peOple with screeN-detected diabetes in primary care study (ADDITION) explored the benefit of early intensive multifactorial treatment in an exclusively screen-detected diabetes cohort (Griffin et al., 2011) . The ADDITION intensive intervention was inspired by the STENO-2 trial (Gaede et al., 2003). In ADDITION, intensive multifactorial treatment over five years period was associated with a non-significant 17% reduction in a composite cardiovascular primary endpoint compared to routine care, but greater improvements in levels of cardiovascular risk factors, 12% reduction in cardiovascular death, 30% for nonfatal myocardial infarction, and 21% for revascularization (Buijsse et al., 2011). These modest results may partly be explained by improvements in the quality of diabetes care during the trial period, a phenomenon that is likely to happen in any screening trial. Nonetheless, ADDITION showed some macro vascular benefits of early treatment for screen-detected diabetes. The extension of the follow-up of the ADDITION study will provide a more definitive answer on the effect of early treatment in people with screen-detected diabetes. In the meantime, data from intervention studies comparing the effects of individual treatment to lower blood glucose (Holman et al., 2008), blood pressure (UKPDS, 1998), and serum cholesterol (Costa et al., 2006, Turnbull et al., 2005), as well as lifestyle modification (Wing et al., 2011) in conventionally diagnosed diabetic populations can inform early treatment strategies with adaptation to suit local settings e.g. adoption of the WHO guidelines for prevention of cardiovascular diseases (WHO, 2007).

Interventions for Prediabetes

The focus of this thesis is on the identification of people with undiagnosed diabetes. However, individuals with IFG and IGT (prediabetess) are a high risk of developing diabetes, any diabetes screening program need to take into account how to manage those at high risk of developing diabetes. This section briefly gives an account of the available treatment options for individuals with prediabetes. Screen detected prediabetes can be managed with lifestyle intervention and/or pharmacotherapy, which have been shown to delay or prevent diabetes in several landmark diabetes prevention trials (Crandall et al., 2008, Gillies et al., 2007). In the

published randomized controlled trials, lifestyle intervention slowed the progression from IGT to diabetes by 30-60%, and this was across a broad range of ethnic groups (Crandall et al., 2008, Gillies et al., 2007). The vast majority of these trials were conducted in populations of developed countries. However, the US Diabetes Prevention Program (DPP) recruited an ethnically diverse population with no racial/ethnic disparities in response rates. In the US-DPP, the lifestyle intervention and metformin reduced diabetes incidence by 58% and 31% respectively, compared with the placebo, after 2.8 years (Knowler et al., 2002), with similar benefits observed in all ethnic groups. Furthermore, two of the diabetes-prevention trials were conducted in populations exclusively from developing countries. The Da Qing study, which enrolled rural Chinese subjects with IGT, demonstrated significant effects of healthy eating, increased physical activity, and weight reduction in decreasing the risk of type 2 diabetes during 6 years of follow up (Pan et al., 1997).

The Indian Diabetes Prevention Program (IDPP) randomized South Asians with IGT to four arms: control (with standard advice), lifestyle modification (diet and exercise), low-dose metformin, and lifestyle modification plus low-dose metformin (Ramachandran et al., 2006). The relative reductions in diabetes incidence were 28.5% with lifestyle modification, 26.4% with metformin and 28.2% with lifestyle modification and metformin (Ramachandran et al., 2006). Results from the diabetes-prevention trials suggest that lifestyle modification would be a much more compelling approach to diabetes prevention in the developing countries such as those in Africa. In addition to effects on diabetes incidence, lifestyle modification also improved cardiovascular risk profile in these trials (Crandall et al., 2008, Knowler et al., 2009, Li et al., 2008). New trials of diabetes prevention are not necessarily needed in developing countries, unless these are setup to address novels questions. Developing countries need implementation studies testing the adaptability of proven diabetes prevention strategies to local conditions. A few community-based translations studies, using culturally adapted individual- and group-based lifestyle interventions delivered by trained lay persons, have been reported in developing countries (Balagopal et al., 2008, Oba et al., 2011). However, these prevention programs have been small in size, were non-randomized studies, and lacked sufficient follow-up to determine the sustained effects of the intervention. Moreover, the lifestyle modification curricula in these studies were not evidence-based, intervention goals were not always specified, and the costs were not evaluated.

3.3.4 Is There a Suitable Test or Examination Acceptable to the Population?

Discussion of the available screening methods for diabetes is based on criteria by Wilson and Jungner, (Wilson J, 1968) which suggests evaluating the efficiency of a screening test by its **validity** (the ability of the test to separate those with the condition sought to those who do not when the test is compared to a gold standard) and **reliability** (the degree to which results obtained from any given test can be replicated). Below is an account of the existing tests to define diabetes. Methods/tests for diagnosing diabetes that are discussed in this chapter include urine glucose, random blood glucose, fasting glucose, glycated haemoglobin, oral glucose tolerance tests and diabetes risk scores.

Urine Glucose

Urine glucose appears to be an inappropriate screening instrument for diabetes given the low sensitivity (16-64%), and positive predictive value (11-37%) (Engelgau et al., 2000). Accordingly, the large proportions of individuals with diabetes are misclassified and remain undetected using this method.

Random Blood Glucose

A study conducted in the US population found that compared to OGTT, a RBG cut-off of ≥6.9 mmol/l considered to be cost-effective exhibits a 93% specificity and a 41% sensitivity (Ziemer et al., 2008). Results of a study conducted in India found that compared to OGTT highest performance in terms of sensitivity and specificity were achieved with a cut-off point of ≥ 7.8 with sensitivity and specificity of 86.5% and 80.7% respectively (Somannavar et al., 2009) . Although RBG is easy to obtain, since it does not require fasting, its performance as a screening tool is limited by the low sensitivity also RBG cut-offs are dependent on the background characteristics of specific populations (e.g., age, sex) and factors like time since last meal, and there may be no universally applicable cut-off.

Fasting Plasma Glucose

FPG is relatively simple (single plasma level measured) and highly correlated with the risk of diabetes complications. It may have modest sensitivity for hyperglycaemia screening. Compared to OGTT, a FPG threshold of ≥7 mmol/l may detect only 55.7% of people with diabetes , but with 100% specificity (Kim et al., 2008). At the recommended optimal cut-off for FPG of >6.1 mmol/l the sensitivity increased to 85.2% but specificity also decreased to

88.5%. For identifying IGT, FPG is not as sensitive as OGTT (Cheng et al., 2006). A FPG threshold of >5.6 mmol/l may detect only 28.9% of IGT cases whereas OGTT would identify 87.4% of cases.

Glycated Haemoglobin

HbA1c has been adopted by the American Diabetes Association (ADA) as a diagnostic test for diabetes at a threshold of ≥ 6.5%. Unfortunately, the ADA criteria for HbA1c do not specifically define IFG and IGT categories, but rather a "high-risk" category corresponding to an HbA1c between 5.7 and 6.4% (ADA, 2013). WHO recommends the 6.5% cut point of HbA1c for diagnosing diabetes, as an alternative to plasma glucose measurements if stringent quality assurance tests are in place and assays are standardized to criteria aligned to the international reference values, and there are no conditions present which preclude its accurate measurement (WHO, 2011b). A value less than 6.5% does not exclude diabetes diagnosed using glucose tests. However, WHO does not make any formal recommendation on the interpretation of HbA1c levels below 6.5% (WHO, 2011b) .

Studies, largely based in Whites have generally indicated a variable performance of HbA1c ≥ 6.5% for type 2 diabetes diagnosis, with an acceptable agreement with ADA/FPG diagnostic criteria (60 to 70%) (Carson et al., 2010, Lorenzo and Haffner, 2010, Cowie et al., 2010), and a lesser agreement with OGTT diagnostic criteria (12 to 30%) (Lorenzo and Haffner, 2010, Cowie et al., 2010, Kramer et al., 2010)). Furthermore the effect of HbA1c ≥ 6.5% on type 2 diabetes prevalence compared to glucose criteria may be ethnicity dependent (Christensen et al., 2010, Cowie et al., 2010) . Indeed, several studies now suggest that race and ethnicity impact on HbA1c, and thus on its performance for detecting diabetes (Christensen et al., 2010, Herman et al., 2007) . Although these racial and ethnic differences remain unexplained, the general trend is that, with everything else being equal, the highest HbA1c values would be recorded among Blacks, followed by Hispanics and then Whites. Studies showing these results have been confined to populations of developed countries.

HbA1c is an appealing screening tool, as it is a stable marker of long-term glycaemic level, does not require to be measured in fasting samples, has values that are not affected by short-term lifestyle changes, may only require a point-of-care testing capillary sample, and has a lower intra individual variability than fasting plasma glucose. However, the costs, unavailability of the test and lack of standardization are limitations to the use of HbA1c

(Saudek et al., 2008). Furthermore, HbA1c tests results can be affected by a number of factors that may be more prevalent in some developing countries such as hemoglobinopathies, other conditions that shorten the lifespan of erythrocytes, iron deficiency, and chronic kidney disease (Gomez-Perez et al., 2010, Herman et al., 2007) . The best cut off points for the diagnosis of diabetes varies across studies with varying sensitivity patterns ranging from 15% in a study in France (Guillausseau et al., 1990) to 92% in Pima Indians (Hanson et al., 1993) , with specificity ranging from 79% in Chinese subjects (Ko et al., 2000) to 100% (Guillausseau et al., 1990) at cut off points ranging from ≥ 5.6 to ≥ 8.6 (Engelgau et al., 2000).

75 g Oral Glucose Tolerance Test

Oral glucose tolerance (OGTT) is currently considered the gold standard for diabetes diagnosis. In addition, it is the only method to formally detect or diagnosed IGT. OGTT identifies about 2% more individuals with diabetes than does FPG (Ramaiya et al., 1991) . However, OGTT has poor reproducibility compared to other glucose-based tests or HbA1c (Ko et al., 1998, Sacks, 2011) . OGTT also has many practical downsides, which are the required 8-hour fast before testing, commitment of staff, and the length of the test itself. For all these reasons, OGTT has been less favoured as a screening test, and is likely to be impractical for African countries.

Capillary Blood (Point of Care) Testing

The simplicity and potentially low cost of capillary blood testing make it appealing for use in low resource settings in developing countries. Nonetheless, the utility of capillary blood testing for screening remains unclear, largely because of concerns of imprecision in the few existing studies and the lack of standardization. An Indian-based study comparing capillary fasting and 2-hour post load blood glucose measurements with fasting and 2-hour post-load venous plasma glucose measurements in screening for diabetes and prediabetess showed a moderate-to-acceptable correlation between a fasting capillary and venous values. Based on the ADA fasting criteria, 31.9% versus 21.1% (capillary vs. venous) had diabetes, whereas based on the WHO criteria, 43.2% versus 38.6% had diabetes (Priya et al., 2011) . In terms of performance at detecting hyperglycaemic states, the C-statistics for prediction of dysglycaemia and diabetes were 0.76 and 0.71 for capillary FPG and 0.87 and 0.81 for venous FPG, respectively in an Australian population (Rush et al., 2008). However, a much

larger study among South-Asians found a much better performance of capillary FPG [C-statistic 0.87 (95% CI 0.81–0.93)] to be significantly better ($P < 0.001$) for C-statistic comparison at predicting diabetes than risk scoring models based upon clinical variables alone [C-statistic for the best clinical model including age, BMI, hypertension, waist circumference: 0.69 (95% CI 0.62– 0.77)] (Ritchie et al., 2011) .

Diabetes Risk Scores

Risk scoring system/questionnaires, particularly the ones not requiring laboratory testing are very attractive solutions for identifying people at high risk of having undiagnosed prevalent or future diabetes, these are discussed in detail in the next chapter on page 49.

3.3.5 Is There a Clear Policy of Whom to Treat as Patients?

For any screening program to be effective a clear policy will need to be in place of whom to treat as patients. The screening policy need to state clearly the aims and objectives of the screening program (WHO, 2003) , whether the aim is to identify; those with pre diabetes, those with undiagnosed diabetes or both . The policy will have to state explicitly the subsequent interventions for each of the outcomes. The screening policy need to state explicitly how the individuals will be identified, what type of tests, define cut off points based on available evidence based on yield , cost effectiveness and availability of resources. The choice of the cut off point for the screening test should bear in mind the capacity of the health system to deal with individuals that will be picked up as high risk that will require a subsequent confirmatory tests and interventions.

3.3.6 Is the Cost of Case Finding and Treatment of Those Found to Have the Disease Economically Balanced with the Health Care Costs in General?

The cost of case finding through screening and the cost of treating those found to have the disease need to be well balanced against the overall health care costs. In Africa especially where there are limited resources with the double burden of diseases it is imperative that the screening programs are implemented in a manner that is cost effective and should be guided by the available evidence such as adaptation of cost effective interventions proposed by WHO for resource limited countries .The available diabetes screening cost effectiveness trial (ADDITION) included a majority of Whites. Moreover, it was conducted in the primary care settings of three European countries where there is good access to care. Implementation of

multiple risk factors intervention used in ADDITION in developing countries may pose challenges related to the lack of a primary care framework to deliver the interventions, and the many gaps in the quality of care for diabetes (Walley et al., 2008).

The health system and infrastructure, especially in a context of competing national priorities may be limitation, however there is evidence of organized diabetes care that could serve as a platform to deliver diabetes screening interventions and management of diabetic and high risk individuals (Echouffo-Tcheugui et al., 2012, Ramaiya, 2005).

Given the higher rates of undiagnosed disease implementing a screening program in an African setting is likely to have a higher yield and confer higher benefits in terms of preventing and managing complications. Thus, implementing screening for hyperglycaemia may require a strengthening of the health systems, which could be challenging. However, a potential benefit of organized screening prediabetess and T2DM is an improvement in the standards of care and treatment for people with diabetes in general and an improvement in the identification of cases and prevention of diabetes complications.

Implementation of prevention programs for individuals of high risk also has its challenges in a system that is mainly focused to providing curative services. There is little information regarding the cost effectiveness and the pragmatism of implementing such programs in the African setting as no research has been conducted in this area. In general, translation of diabetes prevention principles into practice has confronted many challenges (Ali et al., 2012), which may be compounded in developing countries by the lack of qualified investigators, the limited research funding, and the lack of infrastructure. These potential challenges of diabetes translation prevention in developing countries are of many types: First, strategies for identification of high-risk people will have to be clarified. Up till now, diabetes prevention trials have used OGTT to screen for prediabetess, which is impractical for large-scale diabetes prevention programs. Although FPG may be easier, it also presents logistic difficulties for population-based programs. Alternate and practical methods that could be applied in a community setting for identifying people at high risk of type 2 diabetes who would be offered preventative interventions, are risk assessment tools or questionnaires (Buijsse et al., 2011, Noble et al., 2011). These tools will limit the proportion of people that will receive a blood test, and are therefore more practical and potentially economical, however up to now there is no existing risk score that has been developed and validated for use in the African setting. Second, there is a shortage of trained personnel (dieticians,

medical nutritionists, and exercise physiologists) to deliver lifestyle modification in developing countries. However, specialists may not be essential, and lay persons can be trained to deliver physical activity intervention and nutrition counselling, as demonstrated elsewhere (Ali et al., 2012). Indeed, in many US-based studies of diabetes prevention translation, the change in weight among participants was similar regardless of whether the lifestyle intervention was delivered by clinically trained professionals or lay educators (Ali et al., 2012). Third, the intensive individualized approaches used to deliver the lifestyle intervention in diabetes prevention trials may not be practical in real-world setting of the developing world. Hence, community group-based approaches appear as the way forward. Furthermore, models for the delivery of physical activity and dietary interventions would need to use culturally relevant approaches, in order to overcome the potential barriers. Depending on the regions in the developing world these barriers will be of various types. Those related to nutrition include the absence of systematic food labelling and standardized packaging as well as low literacy rates limiting the impact of any food labelling. Barriers related to physical activity are the absence of appropriate infrastructure (e.g., lack of safe walkways, public parks, recreational spaces and cycle trails), environmental obstacles (e.g., high temperatures or humidity in some tropical countries), and limited leisure time to engage in physical activity especially among low-income groups. Other potential obstacles to effective diabetes prevention are cultural perceptions of obesity, as a sign of well-being and thus a source of respect and influence in places like Sub-Saharan Africa (Kamadjeu et al., 2006). Fourth, the cost of rolling-out lifestyle intervention for preventing diabetes may be a challenge (Ackermann et al., 2008). The future benefits prevention of type 2 diabetes to both health-care budgets and the society are clear, but the immediate cost of financing type 2 diabetes prevention programs can be an obstacle in poorer countries (Balagopal et al., 2008). The Diabetes Community Lifestyle Improvement Program (Weber et al., 2011), an ongoing translation trial, should provide more robust data on the effectiveness and cost-effectiveness of diabetes prevention in developing countries.

3.3.7 Are There Programs to ensure that Case Finding is an Ongoing Process?

The screening program has to be an ongoing process for it to be effective. There is no clear evidence to guide the frequency of screening and the age at which to start screening. A study in US suggested that in US screening for diabetes is cost effective when started at the age of

30 to 40 years with screening repeated every three to five years (Kahn et al., 2010). This was a simulated study and not findings from real life study however provides much needed evidence to inform decisions for implementation of screening programs in real life settings. The US, based on ADA guidelines recommends starting screening individuals at the age of 45 (for individuals without compelling risk factors), repeated every three years for those with normal results and yearly for high risk individuals (ADA, 2013). Screening the whole population may not be applicable for low resource countries like those in Africa but considerations for screening those at high risk is imperative. Decisions of who to screen and how often to screen should be guided by the available epidemiological evidence (WHO, 2003). In developed countries because of well-organized health care systems individuals eligible for screening can be identified and invited for screening through the primary health care infrastructure. This is a challenge especially for African countries as no such system exists, use of community health infrastructure and community health workers has proved successful in Africa on other community based interventions such as mass drug administration for neglected diseases, HIV, TB and Malaria programs. Similarly community health workers to could be trained to identify individuals at high risk of diabetes and refer them for screening as per the country's screening policy guidelines.

3.3.8 Approaches for Diabetes Screening

Different approaches for diabetes screening exist; screening the entire population (mass screening) such as the nationwide screening for diabetes that was conducted in Brazil (Nucci et al., 2004), where all individuals above the age of 40 years were invited for screening, about 16% were found to have diabetes. Conducting and sustaining such as screening program is costly especially for poor countries and considerations are needed on the capacity of the health care system to cope with providing care for the identified cases and prevention programs those with prediabetess. Selective multistage screening is another approach which is applied to subjects being identified at high risk after a pre-selection criteria has been applied, an example of which is the Australian Diabetes Screening Protocol (Colagiuri et al., 2004), where risk factors were used as a pre-selection criteria followed by fasting blood glucose, and further testing with OGTT or HbA1c measurement if the fasting glucose was inconclusive. Another example of selective screening is ADDITION screening protocol which was a step wise screening program, that used a combination of diabetes risk factors (a

diabetes risk score) as an initial screening tool, to stratify individuals at high risk, that need to undergo further testing (Griffin et al., 2011). The advantage of the multistage screening is it reduces the burden of having to screen the whole population and rather allows more efficient use of resources, where screening is done on those at higher risk of disease (Mohan et al., 2005, Mohan et al., 2011). Opportunistic screening, is the physician initiated screening where screening is offered to subjects who attend to health care professionals for a reason other than the disorder targeted for screening (Ealovega et al., 2004, Edelman et al., 2002, Fisher et al., 2011, Franciosi et al., 2005, Klein Woolthuis et al., 2007, Klein Woolthuis et al., 2009). This form of screening is of value in settings where the health care system is inefficient for population wide screening such as those in African countries.

3.3.9 Diabetes Screening in Sub-Saharan Africa

Currently there are no specific recommendations for diabetes screening in Sub-Saharan Africa, WHO recommends that countries should have a diabetes screening policy that takes into account the epidemiological (burden of diabetes in the population), health systems (health system capacity to carry out screening, provide effective care to those with and at high risk of diabetes), population (acceptability and psychosocial impact) and economic considerations (WHO, 2003).

Given the increasing burden of diabetes in Sub-Saharan countries and that routine blood tests are not carried out, organised opportunistic screening at health facilities and community gatherings could be an entry point for early case detection for those with undiagnosed diabetes for those at high risk. The burden of diabetes in Africa is now better understood with many more countries now starting to carry out regular surveys for non-communicable diseases, and the data can be used to study the epidemiological pattern of diabetes and other cardiovascular diseases that may help inform the populations at high risk.

The main challenge in initiating screening programs in Africa will be the poor health care systems, for example Tanzania does not implement any organised screening programs but has on going screening services for cervical cancer which is implemented at the health facility level for women who wish to get screened for cervical cancer (Ngoma, 2006, WHO, 2012).

Initiating diabetes screening programs will entail a paradigm shift towards more efficient screening programs that will require investment in the capacity to carry out the screening

(staff training, equipment, and the screening methods) and also improvement in the care facilities for those identified to be at risk or at high risk of diabetes. This could be achieved by integrating the screening into the existing health care facilities rather than introducing diabetes screening as a vertical program.

The screening program by itself could be an opportunity for health system strengthening as a result of increased demand for services. There is lack of data from Africa, but this was observed in Brazil, where more glucose testing was carried out at outpatient laboratories and resulted in strengthening of diabetes prevention and management in primary care facilities following the nationwide community screening in 2001 (Nucci et al., 2004, Toscano et al., 2008), this was a positive impact, although not advocating that a national wide screening is a cost effective way of identifying people with undiagnosed diabetes.

It is unclear how acceptable the screening program will be to the population and the resulting psychosocial effects of labelling individuals to be at high risk or to have diabetes, but there has been quite a success with the HIV screening campaigns with the roll out of voluntary counselling and testing centres. Studies have also shone some light that there are no significant adverse psychological outcomes with screening people for diabetes (Eborall et al., 2007, Park et al., 2008). However given the cultural differences from where these studies were conducted, it is important that appraisal of the screening programs also includes evaluation of program acceptability by both the health workers and the people who are being screened.

The key issue that determines the cost effectiveness of the screening programs is the yield (number detected) of the screening and the costs involved (Icks et al., 2005, Kahn et al., 2010). The costs include the direct, indirect and the opportunity costs. The yield of the program is determined by the protocol used to screen and the resulting sensitivity and the specificity of the chosen screening alogarithm and the post screening interventions to those at high risk and those diagnosed with diabetes. All these factors will need to be put into consideration before initiating screening programs in Africa. Countries will need to generate local cost effectiveness evidence by investing in pilot studies to evaluate various screening strategies based on available evidence from randomised trials.

3.4 Discussion

This chapter discussed the criteria for screening for diseases Vis a Vis diabetes screening. As noted previously there is enough evidence to suggest that diabetes is a growing problem in Africa and the current trends cannot be left unattended. Prediabetess and diabetes are increasingly common in these settings, with high progression rates from prediabetess to diabetes in some populations, and high rates of diabetes-related complications.

Although there is no direct evidence from randomized controlled trials on the effects of treatment of prediabetess, diabetes and its complications from Africa studies from developed countries provide enough evidence on the effectiveness of such interventions to warrant screening for diabetes and prediabetess in high risk individuals (Borch-Johnsen et al., 2003, Echouffo-Tcheugui et al., 2011, Engelgau et al., 2000, Nathan and Herman, 2004, Simmons et al., 2010, Wareham and Griffin, 2001, Waugh et al., 2007, USPSTF, 2003). However, the implementation of these interventions in real-world settings of developing countries can pose a challenge to health systems, which in some cases are delivering suboptimal care.

Several reliable and acceptable biochemical tests that can aid early detection of hyperglycaemic states are available such as the fasting glucose tests, HbA1c and OGTT. The use of random capillary glucose is limited because of the low sensitivity and highly variable cut off points that are dependent on the background characteristics of the population, and the use OGTT has limitation for use as a screening tool because it is a time consuming test and has low reproducibility. Fasting glucose provides a better alternative for the diagnosis of diabetes but there are no data from Africa describing its diagnostic performance and appropriate cut off points vies a vies the gold standard, OGTT and the same applies to HbA1c. Diabetes risk scores provide a cheaper and convenient alternative as an initial screening tool, especially at the primary health care and the community level, but the risk scores tend to be specific to the population from which they were developed and the existing risk scores have limited application for screening in African populations. These would need to be validated and adjusted for use if they were to be applied to the African setting. The performance of point-of-care testing for capillary blood glucose and possibly HbA1c, which is even simpler, less invasive and more convenient than venous testing, deserve further considerations.

Cost-effectiveness of screening for diabetes and prediabetess should be investigated extensively in developing countries. Further studies are needed to look at the yield and the cost effectiveness of various screening algorithms. The aforementioned concerns call for caution when considering a screening program in Africa. However, designing policies for hyperglycaemia screening offers an opportunity to scale-up diabetes care and cardiovascular prevention at large, strengthen the health care systems of developing countries, and thus potentially limit future health care costs.

Chapter 4. Diabetes Risk Scores

4.1 Introduction

A risk score is defined as an objective assessment of the probability of the presence or future development of an adverse health condition based on a combination of risk factors. Risk scores have been used within the field of Cardiovascular Disease (CVD) for many years to estimate the future risk of CVD events and aid clinical decision making (D'Agostino et al., 2008, Kannel et al., 1976). Use of risk scores in the field of diabetes is more recent, with predictions mainly focused on the following outcomes; prediction of prevalent or undiagnosed diabetes (Brown et al., 2012) and prediction of future development of the disease (Buijsse et al., 2011). Some of the scores for example the FINDRISK (Lindstrom and Tuomilehto, 2003) were initially developed for predicting future disease but have also been used to predict undiagnosed or prevalent diabetes (Lin et al., 2009, Rathmann et al., 2005, Witte et al., 2010, Bergmann et al., 2007, Saaristo et al., 2005).

The risk scores can be developed either as computerized algorithm that uses routinely available data in clinical practice to screen for high risk individuals who are then invited for screening, such as the Cambridge diabetes Risk Score (Griffin et al., 2000). Others are developed as simple score questionnaires that can also be used as self-assessment tools by lay individuals (Lindstrom and Tuomilehto, 2003).

The risk scores have been applied in the field of medicine to assess the risk of a particular disease or outcome, based on the level of risk clinicians are able to recommend a specific course of action e.g. behavioural change or specific therapies.

Diabetes risk scores have been used widely as screening tools to identify high-risk individuals who would then be referred for further blood glucose or HbA1c testing. A number of diabetes scores have been developed and published (Brown et al., 2012, Noble et al., 2011, Buijsse et al., 2011). Many of the diabetes risk scores have been developed in developed countries in Whites and Asian populations, It is unclear to what extent a score derived in these populations may be applicable to the African setting.

Given the rising burden of diabetes in Africa and the high proportion of undiagnosed cases and lack of access to diagnostic facilities in this setting, the simple risk scores for undiagnosed diabetes that can be applied in a rural African setting are the focus of this paper. Only simple questionnaire based scores that do not require biochemical measurements are reviewed. The aim of this chapter is therefore to undertake a review of risk scores that are based on self-reported or available clinical data with undiagnosed diabetes as the main outcome, to compare the variables used in the different scores and their performance in derivation and validation populations. This chapter summarizes the finding from review of literature focusing on the diabetes risk scores for detection of undiagnosed type 2 diabetes.

4.2 Methods

4.2.1 Search Strategy

This review was undertaken as part of collaborative work and the methods have been published previously (Brown et al., 2012) with the exception that this report however focuses on the studies that predict diabetes with undiagnosed diabetes as the outcome. My role in the study was from identification of studies to the review write up, my specific tasks during the review process was to extract data and to review the studies methodological quality. Electronic databases (Medline and Embase) were searched for relevant publications on diabetes risk scores, searches were also done on google search engine using the keywords diabetes risk score; also citation tracking was done to identify other articles that may have been missed from the search of the electronic databases. The initial combined search yielded a total of 1029 papers, at abstract stage 123 papers were identified, 74 of those were excluded, 2 more articles were identified later after citation tracking, leaving 51 papers for data extraction (Table 4-1). Eighteen (18) studies on scores that were developed to predict future diabetes as an outcome were excluded (Aekplakorn et al., 2006, Balkau et al., 2008, Kahn et al., 2009, Liu et al., 2011, Gupta et al., 2008, Hippisley-Cox et al., 2009, Schulze et al., 2007, Chen et al., 2010, Chien et al., 2009, Gao et al., 2009, Kolberg et al., 2009, Stern et al., 2002, Sun et al., 2009, Lindstrom and Tuomilehto, 2003, Tuomilehto et al., 2010, Wilson et al., 2007, Schmidt et al., 2005).

Also studies of scores that combine both undiagnosed and diagnosed diabetes as the outcome were not considered (Heikes et al., 2008, Griffin et al., 2000, Bindraban et al.,

2008), Finally 12 studies were included in this study after excluding studies that were only validating other scores and scores that did not have undiagnosed diabetes as their main outcome (Table 4-2). This particular review focused on risk scores that predict undiagnosed diabetes, the decision was made based on the fact that I wanted to compare the score that I am developing to existing scores that predict similar outcomes.

Table 4-1 Search Strategy for Publications on Diabetes Risk Scores

No.	***Search***	***Results***
1	exp Diabetes Mellitus, Type 2/	52918
2	exp Diabetes Mellitus, Type 2/di, ep, pc [Diagnosis, Epidemiology, Prevention & Control]	10157
3	type 2 diabetes.mp.	28837
4	type 2 diabetes.tw.	28836
5	diabetes type 2.tw.	352
6	diabetes type II.tw.	170
7	type II diabetes.tw.	4102
8	exp Diabetes Mellitus/	237369
9	exp Diabetes Mellitus/pc, ep, di [Prevention & Control, Epidemiology, Diagnosis]	47311
10	DM.tw.	16241
11	Non#insulin depend#nt diabetes mellitus.tw.	0
12	non insulin depend#nt diabetes mellitus.tw.	6544
13	NIDDM.tw.	6681
14	adult#onset diabetes.tw.	0
15	adult onset diabetes.tw.	337
16	adult-onset diabetes.tw.	337
17	adult$onset diabetes.tw.	1
18	adult?onset diabetes.tw.	1
19	prediabetess.tw.	220
20	pre diabetes.tw.	220
21	exp Prediabetic State/	2456
22	exp Prediabetic State/ep, pc, di [Epidemiology, Prevention & Control, Diagnosis]	826
23	*Prediabetic State/	1352
24	*Prediabetic State/ep, pc, di [Epidemiology, Prevention & Control, Diagnosis]	362
25	undiagnosed diabetes.tw.	397
26	hyperglyc?emia.tw.	22328
27	exp Hyperglycemia/	17635
28	exp Hyperglycemia/di, pc, ep [Diagnosis, Prevention & Control, Epidemiology]	3468
29	exp Glucose Intolerance/	3764

30	exp Glucose Intolerance/ep, pc, di [Epidemiology, Prevention & Control, Diagnosis]	1191
31	impaired glucose tolerance.tw.	5633
32	IGT.tw.	2231
33	*Glucose Tolerance Test/	4415
34	impaired fasting glucose.tw.	1057
35	IFG.tw.	855
36	dysglyc?emia.tw.	149
37	glucose intolerance.tw.	4859
38	type 2 diabet$.tw.	
39	diabet$ type 2.tw.	
40	type II diabet$.tw.	
41	diabet$ type II.tw.	
42	33 or 32 or 21 or 7 or 26 or 17 or 2 or 1 or 18 or 30 or 16 or 27 or 25 or 28 or 40 or 20 or 14 or 24 or 10 or 31 or 35 or 11 or 22 or 13 or 23 or 29 or 6 or 39 or 36 or 3 or 9 or 41 or 12 or 15 or 38 or 8 or 4 or 34 or 37 or 19 or 5	274599
43	risk score.tw.	2199
44	risk calculat$.tw.	536
45	risk scor$.tw.	2969
46	risk factor calculat$.tw.	6
47	risk scoring method.tw.	8
48	risk scoring scheme.tw.	4
49	risk factor assessment.tw.	339
50	risk equation.tw.	99
51	risk prediction.tw.	1078
52	risk prediction score.tw.	15
53	risk predict$.tw.	1755
54	predict$ score.tw.	275
55	risk function.tw.	195
56	predict risk.tw.	490
57	predict$ risk.tw.	1809
58	project risk.tw.	26
59	project$ risk.tw.	60
60	predictive instrument.tw.	86
61	predictive tool.tw.	331
62	exp Multiphasic Screening/	1046
63	exp Multiphasic Screening/is, mt [Instrumentation, Methods]	74
64	screening tool.tw.	4280
65	(screening adj3 tool).tw.	5345
66	11 or 21 or 7 or 17 or 2 or 22 or 1 or 18 or 23 or 16 or 13 or 6 or 3 or 9 or 12 or 20 or 14 or 15 or 8 or 4 or 19 or 10 or 5	14812
67	42 and 66	923

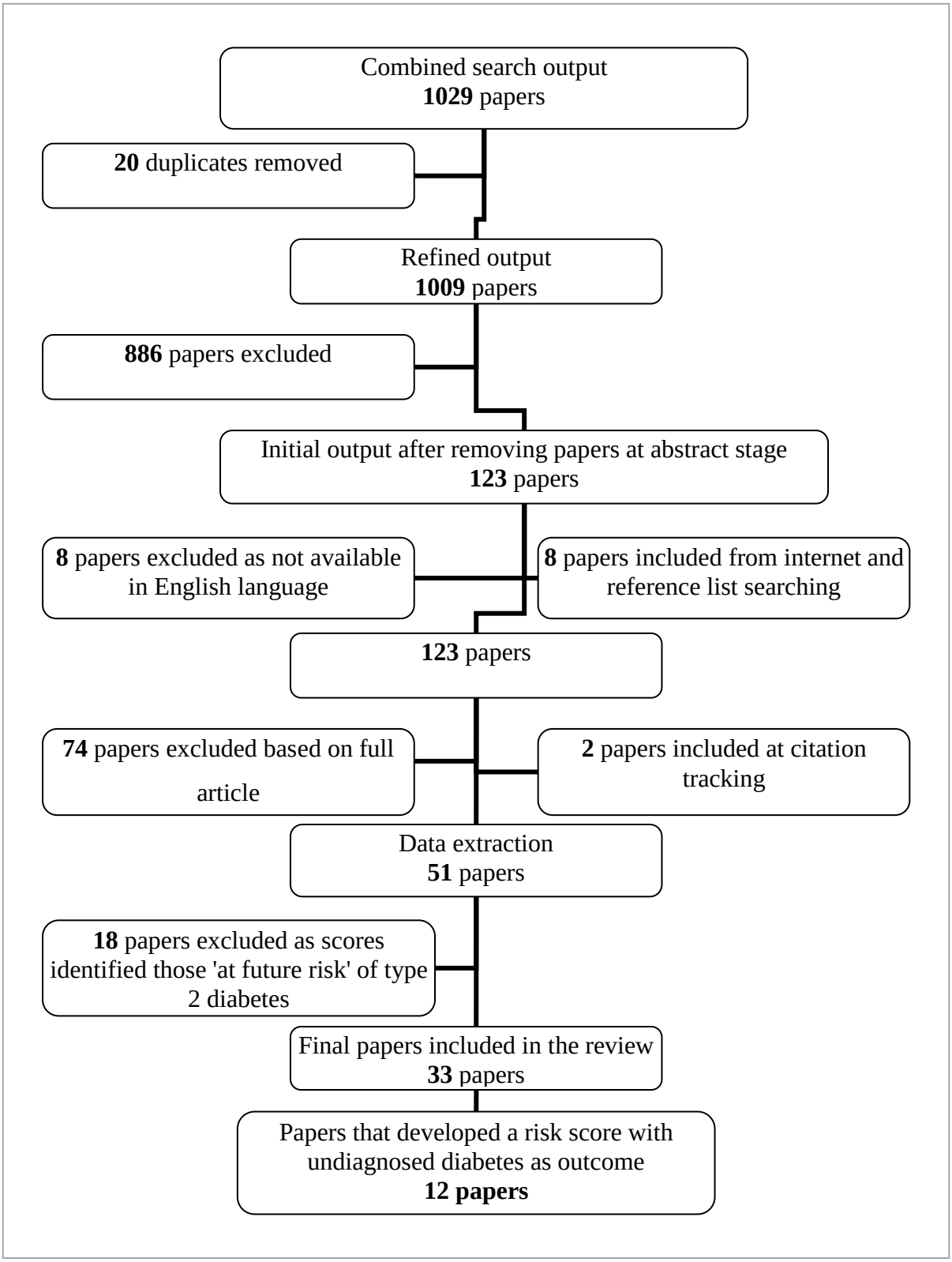

Figure 4-1 Consort Diagram of Summarizing the Selection of Papers Included in the Review of Diabetes Risk Scores

Table 4-2 Criteria Used to Include Studies for the Review of Diabetes Risk Scores

Criteria	Description
Population	- Adults
Intervention	- Screening for type 2 diabetes and, - Questionnaire based screening and, - Abnormal fasting glucose, or impaired glucose tolerance, or undiagnosed diabetes, - Risk score derivation - Undiagnosed diabetes
Outcome	- Sensitivity, Specificity, ROC curve AUC
Study Setting	- Community
Study design	- Any study design with evidence of random selection of participants

4.2.2 Quality Assessment of Studies Included in the Review

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS) is a tool that was developed for assessing quality of studies reporting evaluation of diagnostic tools (Whiting et al., 2003, Whiting et al., 2006). Given that this is a review of risk score screening studies only the applicable items from the QUADAS tool were used in this review to assess study quality. Each item was scored as yes, no or unclear, based in the QUADAS guide for scoring items (Whiting et al., 2003), the description of how each item was scored is attached in Appendix 2. Most of the studies did well on the quality assessment with more that 90% scoring a yes for most of the items, the items which scored poorly are those on description of how the reference test were carried out and whether missing results were explained (item 8 and 9) in Table 4-3 below, which may relate to under reporting of methods in studies rather than the study being of poor quality (Whiting et al., 2006).

Table 4-3 Quality Assessment of the Studies using the QUADAS Quality Assessment Tool

QUADAS Item	Study											
	Ruige (1997)	Baan (1999)	Glumer (2004)	Mohan (2005)	Chaturverdi (2008)	Ramachandran (2005)	Al-Lawati (2007)	Bang (2009)	Gao (2004)	Al khalaf (2010)	Keeskuphan (	Pires de Sousa 2009
1. Was the spectrum of patient's representative of the patients who will receive the test in practice?	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y
2. Were selection criteria clearly described?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3. Is the reference standard likely to correctly classify the target condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5. Did patients receive the same reference standard regardless of the index test result?	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
6. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
7. Was the execution of the index test described in sufficient detail to permit replication of the test?	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y

QUADAS Item	Study											
	Ruige (1997)	**Baan (1999)**	**Glumer (2004)**	**Mohan (2005)**	**Chaturverdi (2008)**	**Ramachandran (2005)**	**Al-Lawati (2007)**	**Bang (2009)**	**Gao (2004)**	**Al khalaf (2010)**	**Keeskuphan (**	**Pires de Sousa 2009**
8. Was the execution of the reference standard described in sufficient detail to permit its replication?	Y	N	Y	N	Y	Y	N	Y	Y	Y	Y	U
9. Were uninterpretable/ intermediate test results reported?	U	U	Y	U	U	Y	N	U	Y	U	Y	U
10. Were withdrawals from the study explained?	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y

Key; Y= Yes, N= No, U= Unclear

Each item was scored as yes, no or unclear, based in the QUADAS guide for scoring items (Whiting et al., 2003), the description of how each item was scored is attached in Appendix 2

4.3 Results

Below are the studies that were identified that met the inclusion criteria, which was of studies reporting development of a risk score to detect undiagnosed diabetes (Al Khalaf et al., 2010, Al-Lawati and Tuomilehto, 2007, Baan et al., 1999, Ruige et al., 1997, Bang et al., 2009, Chaturvedi et al., 2008, Gao et al., 2010, Glümer et al., 2004, Keesukphan et al., 2007, Mohan et al., 2005, Ramachandran et al., 2005, Pires de Sousa et al., 2009) and their results are summarized in Table 4-4 below.

4.3.1 Study Characteristics

The identified studies were from the Netherlands (Baan et al., 1999, Ruige et al., 1997), China (Gao et al., 2010), USA (Bang et al., 2009), India (Chaturvedi et al., 2008, Mohan et al., 2005, Ramachandran et al., 2005), Brazil (Pires de Sousa et al., 2009), Oman (Al-Lawati and Tuomilehto, 2007), Kuwait(Al Khalaf et al., 2010), Thailand (Keesukphan et al., 2007) and Denmark (Glümer et al., 2004) representing mainly Asian and White populations. The score developmental studies ranged from small studies of less than 500 (Keesukphan et al., 2007) participants to larger studies of more than 10,000 participants (Ramachandran et al., 2005) . None of the studies commented on the adequacy of their sample size, which is dependent upon the number of individuals in their sample who have the outcome of interest which is undiagnosed diabetes.

It is recommended that there should be 10 events per variable, for a sample to be adequate for a prediction model (Moons et al., 2012, Steyerberg et al., 2000). For example the Thai risk score (Keesukphan et al., 2007) which has the smallest number of participants, has 3 predictor variables which means for the sample to be adequate at least 30 individuals in the sample should have the outcome translating into a prevalence of about 7%, this information is not provided for the score developmental sample but in the validation sample authors report a prevalence of 13%, which provide enough power to validate the score. With the Kuwaitian score (Al Khalaf et al., 2010), the study population has only 2.3% undiagnosed diabetes among 460 study participants, therefore the sample was inadequate for the selected number of variables (4) in the score therefore subject to affect the performance of the score (Frank E. Harell, 2001, Steyerberg, 2009) . The age of participants among the various studies

also varied considerably. Studies in the Netherlands recruited older individuals above the age of 50yrs (Baan et al., 1999, Ruige et al., 1997), other studies included younger participants, as young as 18years of age (Keesukphan et al., 2007).

Table 4-4 Risk Score for Undiagnosed Diabetes

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
Rotterdam score (Netherlands) (Baan et al., 1999)	a) 1016 b) 55-75 years c) NR d) NR	RPM1 Age, sex, obesity, BP medication RPM2 same as RPM1 plus family history of DM, BMI, physical activity	NR	Age 50-74 RPM1 Cut of point of >6 Specificity 55.0% Sensitivity 78.0% AUC 0.68 (0.64-0.72) RPM2 Cut of point of >36 RPM2 0.74 (0.70-0.78) Sensitivity 72.0% Specificity 55.0%	Oman population (Al-Lawati and Tuomilehto, 2007), age >20 yrs. ; RPM 1 , cut off ≥11, Sensitivity 52.9% to 54.4% Specificity 49.7% to 50.3% AUC 0.53 to 0.54 Kuwait population (Al Khalaf et al., 2010), age >20yrs, RPM 1cut off point >6 Sensitivity 43.0% Specificity 79.0% AUC NR Germany population (Rathmann et al., 2005), age 55-74yrs ; RPM1 cut off >6 Sensitivity 74.0% Specificity 39.0% AUC 0.61 Chinese population (Gao et al., 2010), 20-74yrs, RPM 1 cut off >6 Sensitivity 18.8% Specificity 90.4% AUC 0.63 Taiwanese population (Lin et al., 2009), aged >18yrs, RPM 1 cut off >6 Sensitivity 61.0% Specificity 70.0% AUC 0.69 (0.64-0.73)

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
					US population (Bang et al., 2009), aged >20yrs, cut off >6 Sensitivity 81-89% Specificity 46-55% AUC NR Danish population (Glumer et al., 2006), age NR, Cut off >6 Sensitivity 41.9% Specificity 84.0 % AUC 0.69 (0.65-0.72) Spanish population (Glumer et al., 2006), age NR, Cut off >6 Sensitivity 42.6% Specificity 81.6% AUC 0.66 (0.61-0.71) Australian population (Glumer et al., 2006), age, NR, cut off >6 Sensitivity 49.0% Specificity 82.7% AUC 0.7 (0.67-0.73) US population (Glumer et al., 2006), age NR, cut off >6 Sensitivity 56.5% Specificity 72.0% AUC 0.68 (0.64-0.71) Korean population(Glumer et al., 2006), age NR, cut off >6 Sensitivity 20.8%

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
					Specificity 89.6% AUC 0.60 (0.58-0.63) Asian Population(Glumer et al., 2006), age NR, cut off >6 Sensitivity 11.5% Specificity 92.8% AUC 0.54 (0.49-0.59) African population (Cameroon)(Glumer et al., 2006), Age NR, cut off >6) Sensitivity 16.7% Specificity 91.5% AUC 0.53 (0.48-0.71) Nauru and Tonga populations (Glumer et al., 2006), Age NR, cut off >6 Sensitivity 51.4% Specificity 65.1% AUC 0.62 (0.56-0.66)
Symptoms risk Questionnaire _SRQ (Netherlands) (Ruige et al., 1997)	a) 2364 b) 50-74 years c) NR d) White	Age, sex, pain or shortness of breath during walking, frequent thirst, obesity, family history of DM, BP medication, reluctance to use bicycle for transport	Cut off point >5 Sensitivity NR Specificity NR AUC 0.80 (0.75-0.85)	Age 45-75yrs Sensitivity 72% Specificity 56 AUC 0.69 (0.60-0.79)	None

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
Chinese risk score (China) (Gao et al., 2010)	a)1986 b)20-74years c) 62.7% female d) Chinese	Waist, Age and family history of diabetes	NR	Age 20-74 yrs Cut of point ≥14 Sensitivity 87.0%; Men Sensitivity 80.7%; Women Specificity 27.4%; Men Specificity 47.5% Women AUC 0.63 (0.59-0.68) Men AUC 0.69(0.64-0.72) Women	None
US Risk Score (USA) (Bang et al., 2009)	a)5258 b)>20 years c)NR d)Various	Age, Sex, Family history of diabetes, history of hypertension, Obesity and physical activity	Cut off ≥5 Sensitivity 82.0% Specificity 63.0% AUC 0.79	Age >20yrs Cut point >5 Sensitivity 79.0% Specificity 67.0% AUC 0.74 to 0.83	None
India Clinical Risk Score (India) (Chaturvedi et al., 2008)	a) 4044 b) 35-64yrs c) NR d) Asian Indian	Age, blood pressure, waist circumference, family history of diabetes	Cut off point >16 Sensitivity 66.0% Specificity 67.0% AUC 0.72 (0.68-0.75)	Age 20-69 yrs Cut off point >16 Sensitivity 73.0% Specificity 56.0% AUC 0.69 (0.66-0.71)	None

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
Indian Risk Score (India) (Ramachandran et al., 2005)	a)10003 b)>20years c)NR d)Asian Indian	age, family history of diabetes, BMI, waist circumference, and physical activity	Cut off point >21 Sensitivity 76.6% (70.9-81.7) Specificity 59.9% (58.5-61.3) AUC 0.73 (0.70-0.76)	Age Varied, 3 cohorts Cut off >21 Sensitivity 72.4% to 92.2% Specificity 21.6% to 61.0% AUC 0.67 to 0.73	Chinese population (Gao et al., 2010), aged 20-74, cut off point >21 Sensitivity 96.1% Specificity 18.7% AUC 0.63 (0.60-0.65) Taiwanese population (Lin et al., 2009), aged >18yrs, cut off point NR Sensitivity 63.0% Specificity 69.0% AUC 0.70 (0.66-0.74)
Simplified Indian Risk Score (India) (Mohan et al., 2005)	a) 2350 b)>35 years c)NR d)South Asian	Age, Waist Circumference, family history of DM, physical activity	Cut off point ≥60 Sensitivity 72.5% Specificity 60.1% AUC 0.69 (0.66-0.73)	NR	Kuwait population (Al Khalaf et al., 2010), aged >20, cut off ≥60 Sensitivity 87% Specificity 50% AUC NR
Brazilian Risk Score (Brazil) (Pires de Sousa et al., 2009)	a)1224 b)>35 years c)NR d) Various	age, BMI and Hypertension	Cut off point ≥18 Sensitivity 75.9% Specificity 66.8% AUC 0.77(0.73-0.81)	Brazilian population Cut off point ≥18 85.7% 44.8% AUC 0.72(0.64-0.80)	None
Kuwaitian Risk Score (Kuwait) (Al Khalaf et	a)562 b)>20 years c)52.8%	Age, WC, BP medication, family history of DM	Cut off ≥32 Sensitivity 87.0% Specificity 64.0%	NR	None

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
al., 2010)	female d) Arabic		AUC 0.82 CI not reported		
Thai Risk Score (Thailand) (Keesukphan et al., 2007)	a) 429 b) 18-81yrs c) 63% female d) Thai	Age, BMI and history of hypertension	Cut off point ≥240 Sensitivity 96.8% Specificity 24.0% AUC 0.74	Age 16-80 yrs Cut off point ≥240 Sensitivity 87.1% Specificity 38.0% AUC 0.71	NR
Danish Risk Score (Denmark) (Glümer et al., 2004)	a)6784 b)30-60 years c)NR d)NR	Age, sex, BMI, physical activity, known hypertension, family history of DM	Cut off >31 Sensitivity 73.3% Specificity 74.3% AUC 0.80 (0.76-0.83)	Age 30-60yrs Cut off >31 Sensitivity 66.7% to 75.9% Specificity 72.2% to 73.6% AUC 0.76 to 0.80	Taiwanese population (Lin et al., 2009), aged >18yrs, cut off NR Sensitivity 63% Specificity 70% AUC 0.72 (0.68-0.76) Chinese population (Gao et al., 2010), age 20-74, cut off >29 Sensitivity 55.1%% Specificity 72.1 AUC 0.69 (0.66-0.71) Australian population (Glumer et al., 2005), aged 30-60yrs, cut off >23 Sensitivity 71% Specificity 70% AUC 0.75 (0.71-0.78) Kuwait population(Al Khalaf et al., 2010) , aged >20yrs, Cut off point >31 Sensitivity 39% Specificity 87% AUC NR

Score (Country)	Population characteristics	Variables in the Model	Performance in Derivation	Performance in Validation	Performance in independent Validation
Oman Risk Score (Oman) (Al-Lawati and Tuomilehto, 2007)	a)4881 b)>20years c)57.6% female d) Arabic	Age, Waist Circumference, Body Mass Index, Family history of diabetes and current hypertension status	Cut of point >10 Sensitivity 78.6% Specificity 73.4% AUC 0.83 (0.82-0.84)	Age>20yrs, cut off >10 Sensitivity 62.8% Specificity 78.2% AUC 0.76 (0.74-0.79)	Kuwait population(Al Khalaf et al., 2010), aged >20yrs, cut off >10 Sensitivity 96% Specificity 42% AUC NR Taiwanese population(Lin et al., 2009), aged >18yrs, cut off >10 Sensitivity 65% Specificity 67% AUC 0.72 (0.69-0.75)

Key
a=sample size, b= age of study participants, c= sex, d=ethnicity
NR = Not Reported
AUC = Area under the Curve
RPM = Rotterdam Prediction Model
BMI = Body Mass Index
DM = Diabetes Mellitus
Score performance reported as Sensitivity, Specificity and AUC (95% Confidence Interval)

4.4 Variables Included in the Developed Risk Scores

The identified studies incorporated similar variables. The commonest variables were age and family history. Age was included in all the scores, and was applied as a categorical variable which varied across settings, with the association with the outcome increasing with increasing age across all studies. Family history was included in 10 out of the 12 scores (Al-Lawati and Tuomilehto, 2007, Baan et al., 1999, Bang et al., 2009, Gao et al., 2010, Ruige et al., 1997, Chaturvedi et al., 2008, Mohan et al., 2005, Ramachandran et al., 2005, Glümer et al., 2004, Al Khalaf et al., 2010)

The way family history was measured varied across studies, in some studies family history was reported as any first degree relative with diabetes (Baan et al., 1999, Ruige et al., 1997, Gao et al., 2010, Bang et al., 2009, Chaturvedi et al., 2008, Ramachandran et al., 2005, Al-Lawati and Tuomilehto, 2007) , or parental diabetes history (Glümer et al., 2004, Mohan et al., 2005), or whether only one of the parent has diabetes or both (Keesukphan et al., 2007). In the Kuwait score (Al Khalaf et al., 2010) family history variable is reported as presence or absence of diabetes history in one's siblings . Sex as predictor variable was explored in several studies (Baan et al., 1999, Ruige et al., 1997, Bang et al., 2009, Glümer et al., 2004, Al Khalaf et al., 2010, Pires de Sousa et al., 2009, Ramachandran et al., 2005) but was a significant predictor only in the Dutch (Baan et al., 1999, Ruige et al., 1997) , US (Bang et al., 2009), and the Danish Scores (Glümer et al., 2004).

Measurements relating to anthropometric measures were used in all scores, either measured as Waist circumference (Gao et al., 2010, Chaturvedi et al., 2008, Mohan et al., 2005, Al Khalaf et al., 2010) , BMI (Baan et al., 1999, Ruige et al., 1997, Keesukphan et al., 2007, Pires de Sousa et al., 2009) or both (Bang et al., 2009, Ramachandran et al., 2005, Glümer et al., 2004, Al-Lawati and Tuomilehto, 2007). The variables were included in the model as categorical variables using ethnic specific cut off points.

Hypertension is one of predictors that were incorporated in many of the scores; Hypertension was included in 9 out of the 12 scores. Hypertension was defined as use of hypertensive medication (Baan et al., 1999, Ruige et al., 1997, Al Khalaf et al., 2010), history of hypertension, whether diagnosed previously to have hypertension (Bang et al., 2009, Keesukphan et al., 2007, Pires de Sousa et al., 2009, Glümer et al., 2004, Al-Lawati and

Tuomilehto, 2007). One of the Indian scores, incorporated hypertension as the presence of hypertension at blood a pressure measurement and defines high blood pressure as normal, pre-hypertension and hypertension (Chaturvedi et al., 2008).

Lifestyle variables were also evaluated in some of the studies, including diet, smoking and physical activity/fitness. Physical activity was included in 5 (Baan et al., 1999, Ruige et al., 1997, Bang et al., 2009, Chaturvedi et al., 2008, Mohan et al., 2005, Ramachandran et al., 2005) of the 12 scores. There was wide variability in the way physical activity was measured across settings, with some of the measures being specific to certain settings which may not be universally applicable for example in the Dutch scores (Baan et al., 1999, Ruige et al., 1997) physical activity was assessed as reluctance to use bicycle for transportation. One of the risk scores (Ruige et al., 1997), includes also several symptoms in the model that are predictive of diabetes such as frequent thirst, pain and shortness of breath during walking which are highly subjective and may be difficult to measure consistently across settings and if using clinic data to evaluate risk of individuals in a catchment area like it is being done in certain European settings, the score may be difficult to apply because this information is not available in the clinic databases and the symptoms are rarely specific for example epigastric pain may be described as chest pain.

4.5 Performance of the Risk Scores

Performance of the risk score in this review was assessed using sensitivity, specificity and the area under the ROC curve (AUC), other measures of diagnostic tests performance such as the likelihood ratios, and the measures of calibration were not used because they were not always reported. In presenting score performance statistics, performance in validation represents results of studies reported by the same authors usually done using similar populations to score derivation study population and performance in independent validation, usually across a different setting and by different study teams independent of the score derivation team (Table 4-4).

In the studies included in this review, sensitivity and specificity were reported for all the scores for a specified chosen cut-off point see Table 4-4. The methods for choosing a specific cut of point were not always described. Most studies reported that the cut off point was chosen to maximize sensitivity and specificity.

In some of the validation studies the cut-off points were also modified to fit the new population (Al Khalaf et al., 2010). The highest combinations of sensitivity and specificity for developmental risk scores were 78.6 % and 73.4% achieved by the Oman risk score (Al-Lawati and Tuomilehto, 2007). Sensitivities of the risk scores in developmental populations ranged from 66 (Chaturvedi et al., 2008) to 96.8% (Keesukphan et al., 2007). Only 3 studies reported sensitivity > 80% (Aekplakorn et al., 2006, Bang et al., 2009, Al Khalaf et al., 2010). Specificity for the derivation studies ranged 24% in the Thai risk scores (Keesukphan et al., 2007) to 74.4% in the Danish score (Glümer et al., 2004) respectively. The AUCs for the derivation studies ranged from 0.69 (95% CI 0.66 to 0.73) (Mohan et al., 2005) to 0.83 (95% CI 0.82 to 0.84) (Al-Lawati and Tuomilehto, 2007) indicating good performance in all the scores. In General when the scores were validated within the studies the performances were comparable in sensitivities, specificities and AUCs, there were small differences but their confidence intervals overlapped showing that the differences were not statistically significant (Table 4-4) except for the Oman score (Al-Lawati and Tuomilehto, 2007) which showed lower performance at validation, a concept known as over fitting (Steyerberg, 2009) which may signify that the performance of the model may have been over estimated in the developmental sample.

Of the reviewed risk scores, 5 scores (Baan et al., 1999, Ramachandran et al., 2005, Mohan et al., 2005, Glümer et al., 2004, Al-Lawati and Tuomilehto, 2007) were found to have been independently validated in other populations. The mostly validated score in this review were the Rotterdam (RPM1) (Baan et al., 1999) and the Danish (Glümer et al., 2004) risk scores. The sensitivity and specificity of the validated scores varied greatly across settings and compared to the performance in the developmental sample (Table 4-4). For example the sensitivity of the Rotterdam score (Baan et al., 1999) was 78.0 % in the derivation study but was as low as 11.5% in the validation studies (Glumer et al., 2006) . The score performance in terms of both sensitivity and the AUCs was dependent on the study population with worse performance in populations of African, Asian and Arab origin (Glumer et al., 2006). Thus overall validation studies tended to perform less well than developmental studies. There was no clear evidence that the performance of the scores is related to the number of variables included, a good example is the comparison of the RPM 1 and the RPM2 which showed no differences in the overall performance of the score despite RPM2 having more variables than

RPM1(Baan et al., 1999). Also across other studies risk scores with more variables did not differ in performance any better compared to those with fewer variables (Brown et al., 2012).

4.6 Discussion

This review identified 12 studies exploring the performance of risk scores to identify undiagnosed type 2 diabetes using self-reported or available clinical data.

Many risk scores incorporated similar variables. The score predictive performance was not related to the number of variables included. Some studies did not compare their newly developed score to existing ones to determine if the new score added any further benefit. For example, in India three studies were found (Chaturvedi et al., 2008, Mohan et al., 2005, Ramachandran et al., 2005) incorporating similar variables but none of them validated the existing risk scores already available in India, similarly for the two Netherlands studies (Baan et al., 1999, Ruige et al., 1997). In addition, different studies used different approaches to defining diabetes; most of the studies used FPG and three (Al-Lawati and Tuomilehto, 2007, Glümer et al., 2004, Ramachandran et al., 2005) used OGTT. Overall, these studies found that the published risk scores tested did not differ significantly in their performance based on AUCs which is a measure not affected by the background prevalence of the outcome and other characteristics and so can be used to make comparison across scores. The impact of the diagnostic criteria used to define diabetes and the overall performance of the risk score is unknown as none of the identified studies compared or validated the risk scores based on different diagnostic criteria for diabetes presenting a challenge in comparing the performance of the various scores. The differences in diagnostic criteria did not seem to affect the performance of the risk scores in this review, with studies showing overlapping performances regardless of whether FPG or OGTT was used for diagnosis. None of the scores have been validated using.

Only five scores were independently validated; the Rotterdam (Baan et al., 1999), the Indian (Ramachandran et al., 2005), the simplified Indian (Mohan et al., 2005), the Danish (Glümer et al., 2004) and the Oman (Al-Lawati and Tuomilehto, 2007) risk scores. In general, risk scores developed in one population had less performance when validated in other populations. None of the studies internally validated their scores, therefore it is unclear whether the differences in performance of the scores at validation or were due to actual

differences in the background characteristics of the study population or was due to overestimation of performance in derivation studies (Steyerberg et al., 2001).

Given that the purpose of diabetes risk scores that predict prevalent diabetes is to identify those at risk of undiagnosed type 2 diabetes , the findings of this review suggest that the scores are able to identify those at risk i.e. are able to pick 8 (highest ROC AUC of 0.83 for example) out of every 10 high risk individuals.

Therefore risk scores are a practical approach to stratify individuals at risk during community and outpatient screening through targeted screening, avoiding unnecessary blood glucose or HbA1c measurements.

Studies have shown that those identified by the risk score (true positives) tend to be at higher risk of micro and macro vascular complications than those who are missed (false negatives) and therefore risk scores are suitable as a screening tools (Mohan et al., 2011). However, there is a need to better understand the risks of adverse outcomes in the significant minority of individuals with undiagnosed diabetes who would be missed by the risk score (false negatives). In evaluating screening programs there is need to also look at the outcome of those classified as low risk by the score being used. The yield of the screening tool depend on the chosen cut off point, the less stringent the criteria the bigger the number that will require a confirmatory test and the lower the specificity but higher sensitivity. Depending on the availability of the resources and the aim of the screening program the cut-off point can be adjusted to suit the local needs. The use of a risk score for initial screening to determine who should go on to biochemical testing could therefore be invaluable in poorer countries.

A recent study in India (Mohan et al., 2011), for example, evaluated the use of an OGTT alone, or in combination with the Indian Diabetes Risk Score (Mohan et al., 2005), and showed that use of the risk score followed by OGTT for those at high risk was more efficient and substantially cheaper. The potential benefits in terms of efficiency and costs from using a risk score will be highly dependent on the score's characteristics, particularly its sensitivity and specificity. The Chinese risk score (Gao et al., 2010) for example, had good sensitivity but low specificity (Table 4-4) page 59, yielding a much higher number of false positives and a lower yield for a given number of confirmatory tests. This has resource implications if the

score were to be used as an initial test for screening, resulting in a larger number of people needing a confirmatory test if the published cutoff points are to be applied.

Self-completion questionnaires may also have value as easy to use health promotion tools in low and middle income settings, helping to inform individuals of risk factors for diabetes and providing a potential entry point to lifestyle change. However, more research on the utility of risk scores from this perspective is needed. Also, the use of self completion diabetes risk scores could be limited by the low level literacy as is the case in many developing countries, also the model of delivery would be a challenge with low coverage of postal and internet services, but mobile phone technology could provide a platform for leveraging such health care services.

In conclusion, a number of published risk scores for undiagnosed type 2 diabetes are from Asian and White populations, there is no single score developed for the African population, there is need to develop and or evaluate cost effective approaches to detecting undiagnosed diabetes in this setting.

One approach would be to validate the existing score and update for use in this setting as this review has demonstrated that there is no universally good score, the choice of which score to choose and evaluate in a given population should be driven by pragmatic considerations, based on the setting in which the score would be applied as well as the data and resources available. For example, scores that may require clinical assessment such as blood pressure measurements (Mohan et al., 2005) may not be appropriate in settings where no such services are available. Key resource considerations include the local capacity for diagnostic testing and the effective management of newly identified cases. The other approach would be to develop and validate a diabetes risk score from Africa and evaluate its performance across settings in Africa a process which is being described in this thesis.

The exclusion of diabetes risk score that predict future risk of diabetes could have led to omission of potentially useful scores, but there are no specific recommendations at this stage that states that scores developed to predict future risk can be used to predict prevalent diabetes and vice versa, hower the Finnish diabetes risk score has been validated in several studies for prediction of prevalent undiagnosed diabetes with a slightly lower performance compared to the derivation study but the results were promising. In the Finnish population

when validated cross sectionally the score had an AUC of 0.72 (95 % CI 0.68 to 0.77) in men and 0.73 (95% CI 0.68 to 0.78) in women compared to 0.87 in the original study (Saaristo et al., 2005) . When tested in other populations the Finnish score had an AUC ranging from 0.65 to 0.74 (Bergmann et al., 2007, Gao et al., 2010, Rathmann et al., 2005, Saaristo et al., 2005, Witte et al., 2010). This topic deserves further considerations and further studies to investigate the utility of these risk scores accros different populations.

A major strength of this review was the fact that an extensive search strategy was applied to key databases in addition to text-based queries of internet search engines. Cross-checking of the reference lists of pertinent papers further validated the search findings. The deliberate broad design of the inclusion criteria also facilitated the initial identification of over 1000 studies. Two independent reviewers sifted the data with pre-specified criteria to decide which papers were to be included, performed data extraction, and assessed risk of bias using the QUADAS tool to ensure a standardized approach.

There are also limitations to this review. Firstly, the search strategy only included two electronic databases. It must be acknowledged that searching other databases may have identified other risk score studies. Secondly, only papers available in English were considered. Thirdly the studies used different methods to diagnose diabetes, which may bias the findings of the performance of the scores.

The next chapter will discuss the aims and objectives of this study and the overview of study populations

Chapter 5. Study Aims, Objectives and Overview of Study Populations

5.1 Study Aims and Objectives

5.1.1 Introduction

As mentioned in chapter 2 on page 10 diabetes is an important public health problem in Africa, and many of the diagnosed cases are identified late often with multiple complications and poor survival rates. Diabetes also poses a high economic burden even for developed countries, thus prevention is an important public health strategy in reducing the burden due to diabetes. This study therefore proposes to develop and validate a simple questionnaire based tool that can be used for early identification of those at risk of diabetes for targeted preventive interventions in the African context. Most diabetes risk scores have been developed and validated in Whites and no tool has yet been derived and validated in an African population.

5.1.2 Aim

To develop and validate a diabetes risk score to identify undiagnosed diabetes for African populations, and evaluate its utility within a clinical setting in Tanzania

5.1.3 Objectives

1. To derive a diabetes risk scoring tool from data sets of studies carried out in African populations
2. To externally validate the new risk score in independent populations from Africa
3. To compare performance of the new score with commonly used diabetes risk scores
4. To evaluate the yield, and comment on the cost, of applying the tool in a clinical setting in Tanzania

5.2 Broad Methods

The study had 3 phases: derivation of the risk score tool for detecting undiagnosed diabetes using available population data; validation in independent population data sets and; and validation in a clinical setting. The detailed methods are described in detail in respective chapters.

5.2.1 Deriving the Risk Scores

The risk score was derived from the analysis of data from African diabetes population surveys from Tanzania, Senegal and Guinea. A regression model was built for the diabetes risk factors within the data set, and model coefficients were estimated for the different risk factors. The risk factors with strong association with undiagnosed diabetes were then included in the final model. Each of these risk factors in the final model was assigned a score from which a simple questionnaire was derived based on the predictor variables. The derived risk score was then internally validated to estimate its predictive accuracy within the developmental sample using bootstrap procedure; detailed methods are outlined in chapter six.

5.2.2 External Validation of the Risk Score

The risk score derived above was externally validated in data sets from population based surveys from South Africa, and Guinea. The derived risk score was validated by applying the point based score to the validation studies applying the cut off point which maximised both sensitivity and specificity. More information is found in chapter 7.

5.2.3 Comparison of the New Score to Existing Diabetes Risk Scores

In addition to external validation, the new score was compared with existing scores, by applying the risk scores to the validation data sets using the original cut off points and performance compared using sensitivity, specificity and AUC. Further methods are described in chapter 7 and 8.

5.2.4 Assessing the Score Performance in a Clinical Setting

To assess the score performance in a clinical setting, the score was applied to data collected from screening of diabetes in a clinical setting in Tanzania, where participants were enrolled by invitation. This depicts a setting where the derived tool could be applied. The performance of the score is reported in terms of the sensitivity and specificity and also a comparison of the number needed to screen to identify one case of diabetes when using and not using the risk score. An urban setting was chosen to maximise the yield of individuals with diabetes as studies have shown that prevalence of diabetes was higher in urban settings. Also the chosen study area has well established diabetes care services were individuals who were diagnosed with diabetes were refered for further management. Further details on data collection and

methods are outlined in later in this chaper and also in chapter 8 and also in the field manual attached in appendix 6.

5.3 Obtaining the Data Sets

The data sets for the study was obtained by contacting the study PI's and Co-PI's via email or in person. The investigators were provided with the information about the study and the intended use of the data a description of the variables of interest. The process of obtaining data was quite challenging and took about 2 years to get all the data together, also the Senegal data set was originally in French, I had to have it translated to English before beginning the data analysis process.

The advantage of the data sets was that data was collected using more or less similar methods based on the WHO STEPS guideline with adaptation to suit local settings. The data sets were then modified to uniform variables by redefining the categorical variables as outlined in Table 5-2. The process of combining the categorical variables was more to do with collapsing the different categories to get uniform categories across all studies rather than redefining the variables.

The decision to use a study for either validation or derivation was based on the geographical location of the countries and also the availability of data. For example both the South African data sets were obtained later on in the course of my studies.

5.4 Overview of Study Populations

5.4.1 Introduction

The study data was obtained from studies from 4 different countries in Africa. For risk score development, data was from population surveys of diabetes prevalence in Tanzania, Guinea and Senegal. To assess whether the derived score is applicable to other population, data from diabetes population surveys in South Africa were used to externally validate it. Other sets of data for validation were from a clinical setting in Tanzania and from a cross sectional survey of diabetes in Guinea.

This chapter provides a snap shot of the background characteristics of participants in each study, a brief overview of data collection methods and a summary of study participant characteristics across the studies.

5.4.2 Country Profiles

General background of countries from which study populations were drawn is included in Table 5-1 below. The Republic of Tanzania is an East African country with a population of about 45 million (WB, 2010). The country has a total area of about 947,300 square kilometres almost four times the size of Guinea and Senegal. Senegal lies at the westernmost part of the African continent next to the Atlantic Ocean, at the junction of Europe, Africa and America, with a population of about 12 million people (WB, 2010).

Guinea is a West African country. According to the World Bank Development Indicators Database (2010) (WB, 2010), Guinea has a population of about 10 million people. South Africa on the other hand is located at the southern tip of Africa, with a population of almost 50 million people and a total area of just over 1.2 million square kilometres.

The socio-demographic indicators vary between these four countries (WB, 2010). There is marked difference on the income levels between the countries. Gross Domestic Product (GDP), is a proxy to measure for standard of living/ wealth. The GDP is highest in South Africa. The value of GDP for South Africa (7,280 USD), is almost seven times that of Senegal (1034 USD) and 14 times that of Tanzania (524 USD) and Guinea (452 USD).

The level of urbanisation is highest in South Africa, where 62% of the population is urban, and lowest in Tanzania where almost 80% of the population is rural. Life expectancy at birth is highest in Senegal (57 years) and lowest in South Africa (52 years). The low life expectancy in South Africa despite economic growth could be explained by high HIV prevalence rates that have devastated the country over the last two decades.

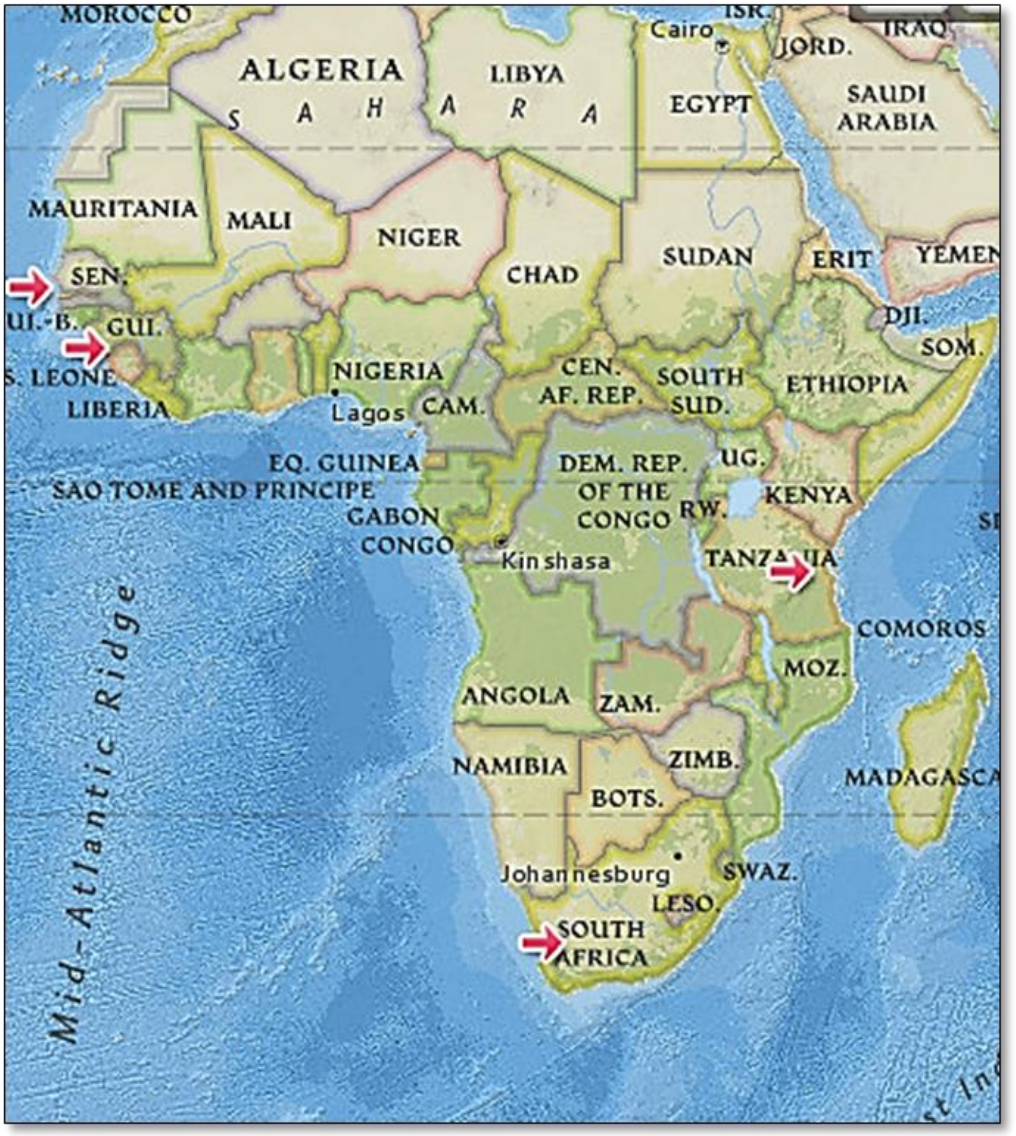

Figure 5-1 Map of Africa Showing Countries Where Data was Obtained for the Study (downloaded from google maps)

Table 5-1 General Background Information Profile of Countries Included in the Study

Indicator	Tanzania	Senegal	Guinea	South Africa
Area of country (Square Km)*	947,300	196,700	245,900	1,219,100
Total population (million)*	44.84	12.43	9.98	49.99
Urban population (% of total)*	26%	43%	35%	62%
Life expectancy at birth (years)*	57	59	54	52
GDP per capita (USD)*	524	1,034	452	7,280
Diabetes prevalence (2011) **	2.8	3.3	4.4	7.1
Diabetes prevalence projections (2030) **	3.5	3.4	4.5	7.4

*Source World Bank Development Indicators Database, 2010 (WB, 2010) **IDF (Whiting et al., 2011)*

The risk of diabetes has been linked to socioeconomic characteristics such as the economic status and the degree of urbanization and the population structure. Tanzania, Senegal and Guinea have comparable estimates with regard to diabetes prevalence at 2.8%, 3.3% and 4.4% respectively (Whiting et al., 2011). South Africa had the highest diabetes prevalence of about 7%, much higher than many other African countries, which could be explained by differences in background characteristics such as the degree of urbanization and exposure to western lifestyle (Mayosi et al., 2012). Prevalence of diabetes is expected to increase globally; of the four countries Tanzania has the highest predicted increment of 25% in prevalence of diabetes by 2030 (Whiting et al., 2011). The section below provides a brief description of data collection methods in each of the studies.

5.4.3 Overview of Data Collection Methods for Studies Used for Deriving the Risk Score

Tanzania Study

This study was conducted as part of non-communicable diseases project by the Temeke Municipality. The study was conducted in Temeke Municipality in Tanzania. Temeke Municipality is one of the 3 districts of the capital city of Dar es Salaam.

Figure 5-2 Map of Tanzania (image downloaded from www.mapsoftheworld.com)

According to the 2002 census Temeke Municipality had an estimated population of 768,451 individuals. The district is mainly sub urban and the majority of its inhabitants are of low socioeconomic status compared to other districts of Dar es Salaam. The Objective of this study was to examine the prevalence of diabetes and other cardiovascular risk factors in Temeke Municipality. This was part of a non-communicable diseases project, which was being implemented by the Municipality.

This was a cross sectional study conducted in 2006. The study enrolled participants aged 24 to 64 years. Cluster random sampling was used to select participants. The primary sampling

unit was the enumeration list from the 2002 census. The secondary sampling units were the ten cell clusters, which were used to sample households. Selection of participants at the household level was done using Kish method. The total sample size was calculated for the study was 1600 participants. A sample size of 768 individuals were calculated based on 5% precision and 95% confidence interval, 50% prevalence and design effect of 2. This sample size was multiplied by two to give sufficient sample size for gender subgroup analyses. 1637 individuals were contacted to participate in the study; a total of 1486 individuals took part, which gives a response rate of 91%. The survey questionnaire used was an adaptation of the WHO STEPS survey questionnaire (WHO, 2009). The questionnaire captured the following; demographic information; behavioral measures on the consumption of tobacco, alcohol, fruits and vegetables and assessment of physical activity. Self-reported information on hypertension, diabetes, dyslipidemia and family history of cardiovascular diseases was also included. In addition the questionnaire also contained measures of socio economic status. Measures of diet and physical activity were also self-reported.

Blood pressure was taken using an electronic sphygmomanometer (OMRON®). Blood pressure was taken at rest, with patient seated and the arm elevated at the level of the heart. The weighing was done in kilograms (kg) with a digital weighing scale (NIKAI®) on a stable and flat surface in a person with light clothing. Height was measured in centimetres, using a folding wooden height ruler. Waist circumference measurements were done using a tape measure using standard methods. Fasting blood samples were taken following an overnight fast. Fasting blood glucose and total cholesterol were measured using an Accutrend® portable machine.

The strength of the study is that this was a population based survey incorporating individuals who were randomly selected for participation in the study. Data collection was done using an adaptation of a standard questionnaire (WHO, 2009) which has been widely used in the African context and therefore is likely to be comparable with studies that have used a similar method.The major weakness of the study is that there were no objective measures of physical activity and the assessment of dietary measures did not use standard validated methods. Use of fasting blood glucose and use of portable meters to define diabetes status, is likely to under estimate the true prevalence of diabetes in this population. The study population is likely to have low prevalence of diabetes being suburban, and may lead to over fitting of the

model in this population due to low number of participants with the outcome (Frank E. Harell, 2001) therefore the findings may not reflect the true performance of the risk score in this population.

The St. Louis Study (Senegal)

The study was conducted by the faculty of Medicine at the University of Sheikh Anta Diop in Dakar Senegal.The study was conducted in the city of Saint Louis. Saint Louis is the former capital of the colony of Senegal, third largest city of the country and second maritime port of Senegal. Saint-Louis has an estimated population of 190,000 inhabitants.

Objectives of this study were to examine the burden of cardiovascular risk factors such as prevalence of obesity, dyslipidemia, hypertension and behavioral risk factors in urban areas of Saint Louis in Senegal.

This was a cross sectional study, conducted in 2010 which included participants 15 years and older. Participants were sampled using clustered systematic random sampling. The sampling frame was represented by data General Census and housing Survey of Saint Louis. A total of 120 clusters of 10 individuals each were taken to constitute the study sample. Sampling was based on probabilities proportional to the size of the primary sampling units. The most populous districts had more clusters. Taking 2% accuracy, a prevalence of 6.7% and a confidence level of 95%, the calculated sample size was 600 individuals. To cancel the effect cluster phenomenon, the estimated minimum sample size required was 1200 individuals. The sudy enrolled a total of 1,424 participants, about 17% more cases than the calculated sample size, with more than 99% response rate for the almost all variables included in the study (Table 5-3).

Figure 5-3 A map of Senegal (image downloaded from www.mapsoftheworld.com)

The survey questionnaire used was also an adaptation of the WHO STEPS survey questionnaire (WHO, 2009) . The questionnaire captured the following; demographic information; Behavioral measures on the consumption of tobacco, alcohol, fruits and vegetables and assessment of physical activity. Included also were questions on background information on hypertension, diabetes, dyslipidemia, general health and family history of cardiovascular diseases.

Blood pressure was taken using an electronic sphygmomanometer (OMRON®). Blood pressure was taken at rest, with patient seated and the arm elevated at the level of the heart. The weighing was done in kgs with a bathroom scale on a stable and flat surface in a person with light clothing. Height was measured in centimetres, using a portable stadiometer .Waist circumference measurements were done using a standard nine metre tape measure, applied directly to the skin. This measure was done at the axillary line, halfway between the lower base of the last rib and the iliac crest on each side.

Participants were invited for laboratory measurements. Blood samples were collected for fasting glucose (FBG), serum creatinine, total cholesterol (TC), HDL cholesterol, triglycerides (TG), and urea and serum creatinine from all individuals and analysed immediately using Reflotron Plus ® (Boehringer Mannheim) machine.

Similarly data were collected using an adaptation of the WHO steps questionnaire (WHO, 2009). The study was conducted in an urban area of Senegal; therefore prevalence of diabetes is likely to be high in this population compared to the Tanzania data, which was collected in a sub urban population, and therefore likely to have high number of people with the outcome of interest.

The weakness of this study is similar to the Tanzania study in respect that diagnosis of diabetes was made using a single fasting glucose measurement. The questions on diet and physical activity were modified to suit that particular population and do not particularly measure the two indices objectively. Findings are therefore likely to be biased.

The Guinea Derivation Study

The study was conducted in collaboration between the Ministry of Health Guinea and University Hospital of Conakry - Donka in Guinea. The overall objective of the study was to conduct a national NCD survey to contribute to the development of promotional programs, a healthy diet, prevention and treatment of hypertension, obesity, diabetes, high cholesterol, smoking and physical inactivity in Guinea. The specific objectives were to describe the current epidemiological characteristics of NCDs and their risk factors in Guinea, to have a representative database for epidemiological surveillance and to collect data to determine the health needs for NCDs.

The study was conducted in the seven administrative regions Guinea (N'Zérékoré, Kankan, Faranah, Mamou, Labe, Boke, Kindia) and Conakry. In total 330 and 303 urban and rural communities were sampled respectively from the regions. The study was a descriptive and analytical observational, cross-sectional study (cross sectional study) on Arterial Hypertension, obesity, diabetes, tobacco use, physical activity and cholesterol.

Figure 5-4 Map of Guinea (image downloaded from www.mapsoftheworld.com)

The study used an adaptation of the STEPS questionnaire (WHO, 2009). The first step (Step 1) concerns the socio-demographic information, measures behavioral issues of physical activity, and food hygiene. The behaviour measures were related to tobacco and alcohol. Questions on health food, consumption of fruits and vegetables were adapted to Guinean habits. In the second (Step 2) the following physical parameters were assessed: height, waist circumference, weighing and blood pressure. Height was measured in centimetres, using a portable measuring board on the floor. Weight was measured in kilograms (kg) and reading taken to the nearest 100g using a balance scale placed on a stable surface, with person dressed in light clothing. Waist circumference was measured using a tape measure, applied directly to the skin, at the axillary line midway between the lower base of the last rib and the iliac crest of each side, the measurement was taken once to the nearest 0.1 cm. Blood

pressure was be taken using an electronics Blood pressure device measured twice. Systolic and diastolic blood pressures were taken on the right arm after 5 minutes of rest without crossing the arms/ legs. In Step 3, four biochemical parameters were measured: fasting glucose, triglycerides, total cholesterol and HDL-cholesterol.Blood glucose is measured using a Hemocue analyser. Triglycerides and HDL-cholesterol were measured only in a subsample of subjects and analysis was done using a Daytona Spectrophotometer ® brand Randox at the Central Laboratory of the University Hospital of Donka-Conakry. Assays were done by enzymatic methods.

Sampling was done using stratified cluster sampling (representative selection of neighbourhoods and districts). To reflect this, the sample size was multiplied by the effect size of the sampling plan. An effect size of 2 (two) was assumed. Available data estimate the prevalence of diabetes in 6% and 8% obesity and hypertension in 30% in rural areas (Balde et al., 2007). With desired precision of 0.05, and Cluster effect of two (2) and anticipated non-respondents of 20% the calculated sample size is approximately 1000 subjects per site rural and urban. Participant eligible for the study were those; aged 25 years or older, residing in the geographic locations (neighbourhood or district) selected, regardless of gender, religious, ethnic or social group and have lived 6 months or more in the selected area. The refusal to participate in the survey was a criterion for non-inclusion in the study.
To account for the assumption of rural gradient / urban distribution in the NCD burden stratification by urbanization was made in each of the natural regions. The criteria for classification urban and rural was the size and population density, accessibility, the traditional way of life, degree of urbanization and the main economic activity.

Geographic locations (urban and rural) were drawn from each stratum. The five primary units were defined in advance. These were the four natural regions (Lower Guinea, Middle Guinea, and Upper Guinea Forest Guinea) and Special Area of Conakry. Secondary sampling units were the districts and tertiary units were the households. The final sampling unit were the individuals whose age is between 25 and 64 years. The study enrolled 2490 participants, 25% more participants than the estimated required sample size, with about 99 % response rates of variables included in the study (Table 5-3).

A procedure for checking the quality of data and quality control was put in place including; validation of the questionnaire and protocol, pre-test, training of investigators, duplicate data entry, Centralization of laboratory tests and quality controls. The research protocol was approved by the National Ethics Committee of the Ministry of Health Guinea.

The strength of this data was that data was a nationally representative sample collected from all administrative regions. Data was collected using an adaptation of the WHO steps tool therefore data can be merged with other studies without the need to redefine variables.

The weakness of the study is that it did not have a family history variable therefore this was not included in the process of developing the model.

5.4.4 Overview of Data Collection Methods for Studies Used for Externally Validating the Risk Score

The Capetown Study (CRIBSA)

The study was conducted by the University of Capetown. The study population involved participants selected from Black African areas of Langa, Guguletu, Crossroads, Nyanga and Khayelitsha townships in Cape Town (Peer et al., 2012).

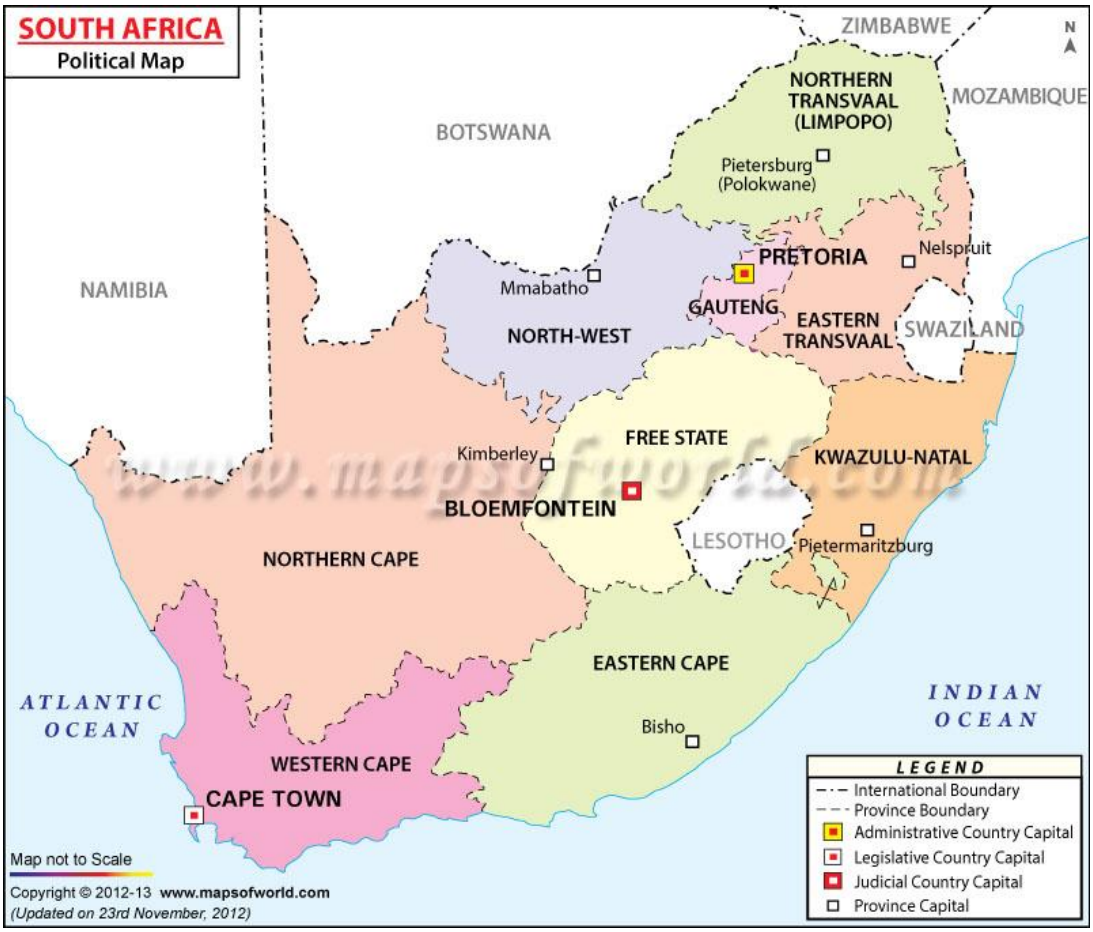

Figure 5-5 Map of South Africa (image downloaded from www.mapsoftheworld.com)

The study sought to; (1) ascertain the prevalence of, and associations with, diabetes in adults living in predominantly black residential areas of Cape Town and to compare these findings with a previous diabetes prevalence study which was conducted in 1990; (2) examine the association between diabetes and psychosocial stress using selected validated questionnaires

This was a cross sectional study. Data were collected in 2008/2009. The target population was 25-74-year-old residents living in the predominantly black African areas mentioned above. These were sampled to provide some overlap with the surveys conducted previously in 1990 (Levitt et al., 1993). The estimated sample size of 1000 was based on an estimated diabetes prevalence of 8% with a precision of 1.5% two-sided with 95% confidence. Participants were sampled using the 2001 census data and aerial maps, a 3-stage cluster sampling stratified by area and housing type was done as follows: stage 1) random sampling of residential blocks within the main strata; stage 2) systematic sampling of plots, flats or structures within blocks; stage 3) individuals from households were selected using quotas for pre-specified age and gender categories. Sampling across the areas and age groups were disproportionate. Langa was oversampled to accommodate a secondary study. Younger age groups were under-sampled and older age groups were over- sampled to ensure at least 50 men and women in each gender category. The following were excluded; unable to give consent, on tuberculosis treatment, on antiretroviral therapy, received cancer treatment within the last year, bed ridden, pregnant or lactating, or resident in Cape Town for less than 3 months. Replacements were allowed when individuals who met the exclusion criteria above refused, or the randomly selected participant of the randomly selected household could not be contacted on the third attempt. The number of participants enrolled in the study was more than the calculated sample size, but the overall response rate for the study is reported to be 86%. For the variables included in this study, the response rate was more than 99% of almost all the variables except for OGTT measurement which had a response rate of 96.2% (Table 5-3).

Fieldworkers administered questionnaires to obtain socio-demographic and migratory information, self-reported medical and family history, physical activity patterns (Global Physical Activity Questionnaire (GPAQ) and tobacco and alcohol use were assessed based on WHO NCD STEPSwise surveillance questionnaire (WHO, 2009). Self-reported food intake during the preceding 24 hours was determined by a single 24-hour dietary recall using semi-structured interviews.

Height, weight, and waist and hip circumferences were measured using standardised techniques (Alberti et al., 2005) . Three blood pressure (BP) measurements were taken at two-minute intervals using an automated Omron® BP monitor with an appropriately sized

cuff after the participant had been seated for five minutes. The average of the second and third BP measurements was used in the analysis.

Blood samples, for glucose were taken after an overnight fast of 10 hours. A standard oral glucose tolerance test (OGTT), using 75 grams of anhydrous glucose in 250 ml of water, was administered, and blood samples taken 120 minutes later. Blood samples were kept on ice and transported to the laboratory within six hours to be centrifuged and aliquoted. Samples were analysed using glucose oxidase method with an auto analyser (Beckman, Fullerton, CA) The strength of this study is that it is also a population survey with participants randomly selected. The study was conducted among black communities and therefore presents an opportunity to validate the score in populations of similar ethnic background as the score derivation data, as studies have suggested coloured South Africans have much higher diabetes prevalence (Erasmus et al., 2001, Omar et al., 1985). The major strength of this study is that the diagnosis of diabetes was made using plasma samples and 2hr OGTT. The OGTT results present an opportunity to validate the score using various definitions of diabetes; fasting alone, fasting and 2hr OGTT and also to look at the performance of the score with regard to identifying cases with Impaired Glucose Tolerance.

The weakness of the study is that older adults were oversampled; therefore the prevalence of diabetes in this population is likely to be an overestimation of the true prevalence of diabetes in black South Africans

The Kwazulu Natal Study

The study was conducted by the University of Kwazulu Natal. Kwazulu Natal is one of the 9 provinces of South Africa (Figure 5-5), densely populated accounting for more than one-fifth of the total South African population. The total population of Kwazulu Natal was, 10,819,100 (2011 estimates). Africans constitute the majority of the population. The study was done in the Ubombo District of rural Kwazulu Natal.

The objectives of the study were to determine the prevalence of diabetes, impaired glucose tolerance, impaired fasting glycaemia and its associated risk factors in a rural South African Black community.

This was a cross sectional study of a predominantly rural South African community. Details of the methods and findings have been published (Motala et al., 2008). The study enrolled individuals more than 15years living in Ubombo district. The estimated sample size was 1300 calculated assuming a prevalence of 9%, and a precision of 2.5% at a 95% confidence level, and adjusting for a 30% non-response rate. The study employed a cluster random sampling method to select households for the survey. Of the total 1300 participants sampled, 1025 (210 men and 815 women) participated, giving an overall response rate of 78.9%. Seventy percent (70%) of the non-responders were men. The response rate for the study variables was over 99% for all the variables included in this study (Table 5-3).

Questionnaires were translated into the local language; interviews were conducted by trained personnel either at the respondent's home or at a local community centre. The questionnaire was developed based on the WHO field guide for diabetes and non-communicable diseases risk factors (WHO, 2009). The questionnaire included questions on socio-demographic information, urbanization, family history of diabetes, and behavioral risk factors such as smoking, current alcohol consumption and physical activity.

Height was measured with a measuring tape to the nearest cm. Weight was measured in light clothing and without shoes, using a floor digital scale to the nearest 0.1 kg. Waist and hip circumference were measured using a flexible tape measure following standard methods (Alberti et al., 2005)

Blood pressure was measured twice, 30 minutes apart, with the participant sitting, using a sphygmomanometer; the mean of the 2 readings was used in the analysis.

All participants underwent Oral Glucose Tolerance measurement. Venous blood samples were drawn after an overnight fast and 2 hours after the ingestion of 75g glucose load dissolved in 250 mls of water. The blood samples were then kept on ice, transported to the lab and centrifuged within 6 hours of collection. The separated plasma was stored at -30 degrees until analysis. Plasma glucose was determined using glucose oxidase method Boehringer Mannheim (Mannheim, Germany).

The strength of this study is that it was a population based study with random selection of participants. Diagnosis of diabetes was also based on 2 hr OGTT and therefore provides good estimates of diabetes prevalence.

The main weakness of the study is that the study has an overrepresentation of female participants; almost 75% of respondents were females. The higher percentage of female respondents could affect the performance of the score in this population, because of possible differences between sexes in various diabetes risk factors such as obesity, physical activity levels etc.

Tanzania Validation Study

Data for this study was collected as part on my PhD study. The study was conducted in Dar es Salaam region, in Temeke, Mwananyamala and Amana Municipalities. Participants were recruited at the 3 Municipal Hospitals following invitations to participate using posters and outreach mobile vans that were sent to the communities around these 3 hospitals. The objective of this was to collect data to evaluate the performance of a diabetes risk score within a setting where individuals are freely invited to participate. This was a cross sectional study conducted in 2011 to 2012. Participants aged 34-65 were invited. Details of methods are included in Appendix 6.

The total sample size calculated for the study was 1200 participants. The sample size was calculated based on the minimum number of patients with the outcome and the expected prevalence. About 1081 people were enrolled to the study, with the overall response rate of 90% and about 99% response rates to almost all the variables included in the study see Table 5-3. Data were collected by 2 to 3 study nurses in each site who had been previously trained on diabetes, and received a 2 days training on the questionnaire and how to perform the physical measurements for the study. Blood and urine samples were collected by the study laboratory assistant. The main challenge for the data collection was having to supervised 3 different data collection sites; a decision was then made to collect data from the sites on alternate weeks after the first week of data collection.

The survey questionnaire used was an adaptation of the WHO STEPS survey questionnaire (WHO, 2009). The questionnaire captured the following; demographic information; behavioural measures on the consumption of tobacco, alcohol, fruits and vegetables and

assessment of physical activity. Self-reported information on hypertension, diabetes, dyslipidemia, and family history of cardiovascular diseases was also included. In addition the questionnaire also contained measures of socio economic status, diet and physical activity which were also self-reported. Blood pressure was taken using an electronic sphygmomanometer (OMRON®). Blood pressure was taken at rest, with patient seated and the arm elevated at the level of the heart.

The weighing was done in kilogram (kg) with a digital weighing scale (SECA®) on a stable and flat surface in a person with light clothing. Height was measured in centimetres, using a portable stadiometer (SECA®). Waist circumference measurements were done using a tape measure using standard methods (Alberti et al., 2005).

In addition to the questionnaires and physical examination, patients were requested to return to the clinics to provide fasting blood sample for blood glucose, creatinine and cholesterol measurements, as well as bring morning urine samples for urine albumin and creatinine measurements. Patients were instructed to fast for at least 8 hours before the test. All tests were performed by a trained technician. Blood was taken by finger prick, and measured using Hemoque® 201 analyser.

Blood was also taken for lipid measurements; High Density Lipoprotein Cholesterol (HDL), Total Cholesterol (TC), and triglycerides (TG) and Creatinine. Four mls of venous blood was drawn from anterior cubital fossae, and placed in a plain vacutainer. Blood was kept at room temperature and was analysed the same day, within hours of sample collection. Samples were analysed using fully automated biochemistry analysers by the direct end point enzymatic method.

Patients were instructed to bring morning urine samples, after providing them with a sterile urine container, samples were analysed on the same day of collection, if the samples could not be analysed within hours of collection, they were refrigerated and analysed within days after allowing returning to normal temperature. Prior to analysis of albumin and creatinine, samples were screened for infection and overt proteinuria using MULTISTIX® 10 SG strips. Those found to have blood traces, leucocytes or protein were excluded. Samples were then analysed for albumin and creatinine using CLINITEK® Microalbumin Reagent Strips on the CLINITEK STATUS® urine analyser. The two values were used to calculate albumin

creatinine ratio. Albumin Creatinine ratio was classified into normal (<30mg/g), microalbuminuria (30 to 300mg/g) and macroalbuminuria (>300mg/g) (Sacks et al., 2002).

A third of the patients at Mwananyamala hospital underwent Electrocardiography (ECG) measurements (12 lead ECG) using a MAC® 1200 ECG machine. However due to time constraint these were not analysed and therefore the finding are not included in this report

Data was entered using Epi Data Software, the data entry questionnaire was designed with checks to ensure that incorrect entry are minimised for example the probable minimum and maximum values for continuous variables. The data was then exported to STATA 12 software for cleaning and analysis.

The strength of the study is that data were collected using an adaptation of standard questionnaire which has also been used by a number of studies including those included in this study. The study has a number of variables that can be used to compare the yield of scores across different outcomes of interest, such as micro-albuminuria and lipids levels.

The major weakness of the study was that participant enrolment was by convenient sampling where individuals fitting the inclusion criteria were invited to participate therefore more likely to attract individuals at high risk, and hence more likely the score will have more yield than if the score were to be applied to a general population selected at random. Also the results of the study may be biased and therefore can not be generalised to the Tanzanian population.

The Guinea Validation Study

The study was conducted by University Hospital of Conakry - Donka in Guinea. Guinea is a West African country with a tropical climate. At the time when the study was conduted in 2003, according Guinean census, the population was made up of 7156,406 inhabitants with 49% men and 51% women. The rural population was estimated at 70% of subjects and 60% of Guineans are under 20 years of age.

Futa Jallon province, in the north of the country, had a population of 1639,617 inhabitants and the Fulani represent the predominant ethnic group. Labé, the largest city in Futa Jallon, was selected for the urban survey while Fellö-Koundoua (in the prefecture of Tougué) was chosen for rural sampling. Labé is the fourth largest city in Guinea, situated 431 km north-

east of Conakry with a population of 79,347. Fellö-Koundoua is 193 km further north, between Labé and Tougué, and has a population of 5932. Choice of this latter site was based on criteria defining its rural situation (isolation, difficulty of access by road, low levels of infrastructure, traditional lifestyle and diet) contrasting with that of the urban zone of Labé (Figure 5-4).

Objectives of the study were to study the prevalence of diabetes and its associated risk factors. This was a cross sectional study, conducted in February 2003 , methods and results of which have been published previously (Balde et al., 2007). A sample size of 384 was determined, based on an estimate of diabetes prevalence of 50%, to obtain an absolute precision of 5% for the 95% confidence interval. This sample size was multiplied by the maximum design effect for clustering of two to give a sample of 768. To allow for a non-response rate of 30%, a final sample size of 1000 per community was employed. Houses were randomly selected from the list of the Guinean census. All residents of these houses aged 35 years and over were invited to take part in the study. Non-participation linked to absence was recorded after two visits to the household. The overall participation rate was 70% with 1537 of the 2000 individuals who were to be enrolled.

After informed consent was obtained, subjects were taken through a questionnaire administered in one session which recorded name, age, sex, ethnic group, medical history, obstetric history and family history of diabetes mellitus. The questionnaire was orally translated into Fulani for persons who did not understand French Height was measured with a measuring tape to the nearest cm. Weight was measured in light clothing and without shoes, using a floor digital scale to the nearest 0.1 kg. Waist and hip circumference were measured using a flexible tape measure. After at least 10 min rest, blood pressure was measured in the right arm of seated subjects on two occasions, at an interval of 1 min, using an appropriate size sphygmomanometer. Subjects were examined during the morning after fasting since the previous evening meal. Capillary whole blood was obtained from a finger puncture and was immediately analysed using a Hemocue blood glucose analyser (Hemocue® AB, Box 1204, 26223 Angelholm, Sweden).

Strength of the study is that the study enrolled participants randomly and there was a uniform data collection tool using STEPS methods.

5.4.5 Summary of the Studies

Summary of Study Characteristics

The score derivation cohorts included participants from cross sectional studies. The studies included participants from rural, peri-urban and urban areas. The studies enrolled participants aged 15 years and above. The derivation cohort comprised of a total of 5411 participants, 1496 (27.6%) from Tanzania, 1424 (26.3%) from Senegal and 2490 (46%) from Guinea respectively. The surveys were carried out from 2006 to 2011 based on the WHO STEPS methods for chronic non-communicable disease research. Information from participants was obtained by interviewer administered questionnaires and physical measurements were performed by trained personnel. Information on lifestyle factors such as physical activity and smoking were self-reported. Table 5-2 summarizes how each of the categorical variables was coded in the data sets.

Physical activity was assessed using the GPAQ in Tanzania and Guinea data sets where participants were asked about the domains (leisure, work, commuting), number of days (frequency) and intensity of physical activity. In the Senegal survey the assessment was based on the type of physical activity that participants engaged with. Regarding smoking behaviour participants were asked whether they were current/ past smoker or non-smoker. History of high blood pressure and diabetes was ascertained by asking participants whether they have ever been diagnosed with the condition by a health care worker. Presence of hypertension was defined as a positive history of hypertension and or systolic blood pressure of more or equal to 140 mmHg and or a diastolic blood pressure of more or equal to 90 mmHg. Family history of diabetes was assessed by asking participants about history of diabetes in their first degree relatives (parents, children or siblings). Information on family history of diabetes was only available for the Senegal data. In all the derivation studies blood glucose was measured by a single fasting blood glucose measurement.

Four studies were used to validate the score and to compare performance of the newly developed score to existing diabetes scores for predicting prevalent diabetes. Three of the studies used for validation are community based studies; these include the 2 South Africa studies and the Guinea study. The Tanzania validation study was a hospital based study where individuals were invited for screening, depicting a typical clinical setting where the

score could be applied to screen individuals at high risk. Two of the studies are from South Africa, one conducted in a rural black community in Kwazulu Natal where a total of 1025 participants were enrolled and the other from a predominantly black community in Cape Town in 2008 with a total of 1116 participants. The Tanzania and Guinea validation studies had a total of 1081 and 1537 participants respectively. Assessment of lifestyle measures and other categorical variables were the same as described for the derivation studies except for physical activity in the South African studies where it was assessed as leisure and occupational physical activity. Occupational physical activity was assessed by intensity only, where participants were asked to rate their occupational physical activity as either sedentary, light, moderate, or vigorous and leisure physical activity was assessed by frequency ranging from never to more than 3 times a week, Table 5-2. In the validation studies blood glucose was measured by fasting and oral glucose tolerance test; (OGTT) in the 2 South African studies and by fasting glucose alone in the Tanzania and Guinea validation studies.

The different studies used different diagnostic criteria for diagnosing diabetes; the studies that used fasting glucose alone might have underestimated the true prevalence of diabetes in the studied populations and therefore may affect the overall performance of the score in the populations but given that also in the derivation studies the diagnosis of diabetes was done based on fasting glucose alone, the risk score comparisons are done based on the fasting glucose. In addition OGTT is also used as the gold standard in evaluating the performance of the risk score in the South Afrcan validation studies, given that fasting glucose and OGTT identify different spectrum of people the performance of the score is likely to be different between the two groups.

Completeness of Data

Table 5-3 shows a summary of the availability of data across countries for all variables used in the analysis. The studies overall had good response rates of more than 80%, except for the Guinea study that was used for validation which had a low response rate of 70, there is no available data on the individuals who did not participate in the Guinea study to make possible comparisons with those who participated.

Attempts were made to analyse the pattern of missing data using the *misstable* command in STATA in the different data sets and these revealed that the data were missing completely at

random (MCAR) , there were no specific patterns of missing data that were observed. Since data were missing at random and only about < 5% of the data were missing, complete case analysis was done for both model derivation and validation. Although complete case analysis is acceptable with low levels of missing data, it could introduce bias since not all the information is available for the analysis, and may reduce statistical power if many cases are left out in the analysis.

Table 5-2 Categorical Variable Coding in Derivation and Validation Data Studies

Variable	Derivation studies			Validation studies				
	Tanzania	**Senegal**	**Guinea**	**CRIBSA**	**KZN**	**Tanzania**	**Guinea**	**Combined**
Education level	Less than primary/ primary/secondary/ college/graduate /post graduate	Less than primary/ primary/secondary/ college/graduate /post graduate	No formal schooling/ Less than primary school/ Primary school completed/ Secondary school completed/ High school completed/ College/University completed/ Post graduate degree	No variable	No variable	No formal schooling/ Less than primary school/ Primary school completed/ Secondary school completed/ High school completed/ College/University completed/ Post graduate degree	No formal schooling/ Less than primary school/ Primary school completed/ Secondary school completed/ High school completed/ College/University completed/ Post graduate degree	Less than primary/primary/secondary/tertiary
History of high Blood Pressure (ever told by health worker)	(yes/no)	(yes/no)	yes/no	Yes/ No/ Don't know	Yes/ No/ Don't know	Yes/No	Yes/No	Yes/No
Physical activity	Participate in occupational or leisure; moderate/Vi	Participate in physical activity (Yes, No) Type of	Participate in occupational or leisure; moderate/Vigorous physical activity	Occupational physical activity; sedentary/ light/moderat	Occupational physical activity; sedentary/ light/modera	Participate in occupational or leisure; moderate/Vigorous physical activity	Participate in occupational or leisure; moderate/Vigorous physical	Variable omitted in model derivation, used in validation

Variable	Derivation studies			Validation studies				
	Tanzania	**Senegal**	**Guinea**	**CRIBSA**	**KZN**	**Tanzania**	**Guinea**	**Combined**
	gorous physical activity (yes/no) days and duration	physical activity Number of days and duration	(yes/no) Number of days and duration	e/heavy Leisure physical activity; never/ < once per wk/ 1-2 times per wk/ 3+ times per wk	te/heavy Leisure physical activity; never/ < once per wk/ 1-2 times per wk/ 3+ times per wk	(yes/no) Number of days and duration	Activity (yes/no) Number of days and duration	
Tobacco	Current, Daily, past smoker (yes /no) Number and type	Current, Daily, past smoker (yes /no) Number and type	Current, daily, past smoker (yes /no) Number and type	Yes/ No /ex-smoker	Yes/ No /ex-smoker	Current, Daily, past smoker (yes /no) Number and type	Current, Daily, past smoker (yes /no) Number and type	Never/ current/past smoker
History of Diabetes	Yes/ No	Yes/No	Yes/ No	Diabetes 1=yes 2=no	Diabetes 1=yes 2=no	Yes/ No	Yes/ No	Yes/No
Family history of diabetes	No variable	Yes/No	No variable	Yes/No	Yes/No	Yes/No	No variable	Variable not used in validation

Table 5-3 Pattern of Missing Data in the Derivation and Validation Studies

Characteristic	Derivation				Validation			
	Overall	Tanzania	Senegal	Guinea	CRIBSA	KZN	Tanzania	Guinea
N	5411	1496	1424	2490	1116	1025	1081	1537
Age	100%	100%	100%	100%	100%	99.8%	100%	100%
Sex	100%	100%	100%	100%	100%	100%	100%	100%
Waist Circumference	99.3%	97.9%	99.9%	99.8%	99.9%	99.3%	98.8%	100%
BMI	99.3%	99.5%	99.8%	99%	100%	99.2%	97.4%	100%
History of Hypertension	100%	100%	100%	100%	100%	99.8%	99.9	-
Mean SBP	99.7%	99.2%	100%	99.9%	99.8%	99.8%	99.4%	100%
Mean DBP	99.7%	99.2%	100%	99.9%	99.8%	99.8%	99.4%	100%
Smoking	99.9%	99.9%	100%	100%	100%	99.8%	100%	-
FBG	-	92%	-	98.1%	98.6%	99.6%	96.7%	100%
2hr OGTT	-	-	-	-	96.2%	96.6%	-	-
History of Diabetes	100%	100%	100%	100%	99.9%	100%	99.9	100%
Family History of diabetes	-	-	100%	-	100%	100%	99.5	-
Physical activity	98%	100%	95.2%	99.0%	99.7%	99.8%	99.2%	-
Smoking	100%	100%	100%	100%	100%	99.8%	100%	-
Education level	99.9%	100%	100%	99.9%	-	-	100%	-
Diabetes diagnosis	-	-	100%	-	-	-	-	-

5.4.6 Characteristics of Respondents in the Derivation and Validation Studies

Table 5-4 shows the summary characteristic of study respondents for both the derivation and validation studies. The mean age for the derivation studies ranged from 34.1 years to 43.6 years, with Senegal having the lowest mean age across the 3 countries. Over all mean age for the combined derivation cohort were 39.2 years and 47.1 years for the validation studies. The mean age for the validation studies ranged from 43.9 years in the Cape Town (CRIBSA) study to 49.4 years in the Guinea study. Overall participants of all studies were mostly female, highest being the Kwazulu Natal study where almost 80% of study respondents were female. In score derivation studies the mean waist circumference ranged from 82.0 cm to 85.4 cm in the Guinea and Tanzania studies respectively, with a mean of 83.6 cm in the combined score derivation data set. In the validation studies high mean waist circumference is reported in the CRIBSA and Tanzania study with mean waist circumference of 93.2 cm and 93.3 cm respectively. Mean BMI values follows a similar pattern as the waist circumference with highest mean BMI of 26.0 kg/m2 in the Tanzania study and the lowest mean BMI of 22.9 kg/m2 in Guinea study among the derivation studies. For validation studies BMI ranges from 22.7 kg/m2 in the Guinea study to 29.9 kg/m2 in the CRIBSA study. In the derivation studies hypertension was highest in the Senegal study with 44.2% of participant being classified as hypertensive by blood pressure measurements, and 23% of their study participants had a prior history of hypertension. Mean systolic (135.5 mmHg) and diastolic blood pressure (87.9 mmHg) was also highest in the Senegal study compared to other derivation studies. Among the validation studies highest prevalence of hypertension was in the Tanzania study, with 26.7% of respondents having prior history of hypertension and 36.6% being classified hypertensive upon blood pressure measurement, with mean systolic and diastolic blood pressure of 134.3 and 81.1 mmHg respectively.

The prevalence of diabetes varies greatly in the various populations used in this study. For the derivation studies the prevalence of diabetes ranges from 3.6 % in Tanzania to 10.4% in Senegal and in validation studies the prevalence of diabetes ranges from 4.4 in the Kwazulu Natal study to 14.9 in the Tanzania study.

Table 5-4 Summary of Participants Characteristics in the Derivation and Validation Studies

Characteristic	Derivation				Validation				
	Overall	**Tanzania**	**Senegal**	**Guinea**	**CRIBSA**	**KZN**	**Tanzania**	**Guinea**	**Overall**
N	5411	1496	1424	2490	1116	1025	1081	1537	4759
Age in years (SD)	39.2 (15)	43.6 (11.4)	43.4 (17.8)	34.1 (13.6)	43.9 (13.1)	46.9 (18.9)	47.1 (12.4)	49.4 (12.9)	47.1 (14.5)
Sex (% Male)	2259 (41.7%)	676 (45.3%)	441 (31%)	1140 (45.8%)	399 (35.8%)	210 (20.5%)	347 (32.1%)	730 (47.5%)	1656 (35.4%)
Waist Circumference in cm (SD)	83.6 (13.7)	85.4 (13.1)	84.6 (15.9)	82.0 (12.7)	93.2 (15.5)	85.6 (13.2)	93.3 (14.5)	76.7 (11.5)	86.2 (15.4)
BMI in kg/m^2 (SD)	24.4 (5.8)	26.0 (5.7)	25.5 (6.4)	22.9 (5.0)	29.9 (8.4)	25.2 (6.7)	27.2 (6.0)	22.7 (3.8)	25.9 (6.8)
[∞]Hypertension, n (%)	1930 (35.7%)	542 (34.5 %)	628 (44.2 %)	760 (30.5%)	365 (32.5%)	270 (26.5%)	394 (36.6%)	483 (31.4%)	1512 (31.7%)
Hypertension History, n (%)	803 (14.8 %)	270 (18.0 %)	328 (23 %)	205 (8.2%)	342 (30.6%)	167 (16.3%)	288 (26.7%)	-	-
Mean SBP (mmHg)	131.2 (22.6)	131.7 (23.1)	135.5 (26.7)	130.9 (22.3)	126.2 (23.3)	126.3 (27.7)	134.3 (25.6)	126.9 (25.1)	128.3 (25.5)
Mean DBP (mmHg)	82.6 (13)	82.3 (13.0)	87.9 (15.4)	79.0 (13.1)	82.0 (13.2)	80.0 (17.3)	81.1 (14.1)	78.9 (12.5)	80.3 (14.2)
Smoking									
Never , n (%)	4459 (82.5 %)	1224 (81.9 %)	1213 (85.2%)	2022 (81.2%)	-	866 (84.7%)	992 (91.8%)	-	-
Former (%)	398 (7.4 %)	125 (8.4 %)	117 (8.2%)	156 (6.3%)	-	29 (2.8%)	53 (4.9%)	-	-
Current (%)	551 (10.2 %)	145 (9.7%)	94 (6.6%)	312 (12.5%)	297 (26.6%)	128 (12.5%)	36 (3.3%)	-	-

Characteristic	Derivation				Validation				
	Overall	Tanzania	Senegal	Guinea	CRIBSA	KZN	Tanzania	Guinea	Overall
Mean FBG in mmol/l (SD)	-	4.6 (2.2)	-	4.6 (1.5)	5.4 (2.5)	4.9 (1.5)	5.3 (3.5)	5.1 (2.0)	5.2 (2.5)
Mean 2hr OGTT in mmol/l (SD)	-	-	-	-	6.9 (4.2)	6.2 (2.5)	-	-	-
Total Diabetes, n (%)	327 (6.2 %)	49 (3.6%)	148 (10.4%)	130 (5.3%)	142 (12.1%)	46 (4.4%)	156 (14.9%)	94 (6.1%)	438 (9.2%)
New Diabetes, n (%)	143 (2.7%)	35 (2.5%)	37 (2.6%)	71 (2.1%)	40 (3.7%)	40 (3.9%)	99 (9.4 %)	66 (4.3%)	245 (5.1%)

Key
[∞] Hypertension is defined as SBP>=140 and or DPB >=90
SD = Standard Deviation
SBP = Systolic Blood Pressure
DBP = Diastolic Blood Pressure
FBG = Fasting Blood Sugar
OGTT = Oral Glucose Tolerance
BMI = Body Mass Index
N = Total number of participants in the study
n = Number of participants

5.5 Discussion

This chapter provides a description of studies and characteristics of study participants in the studies used for deriving and validating a risk score for use in the African population. The review of the methods show that data collection methods were comparable across all studies, using the WHO recommended methods of data collection. Although there were slight differences in how data for various lifestyle measures were collected, the variables could be categorized into uniform variables across all studies, with the exception of physical activity and diet which was not considered at all because of differences in methods of data collection and the lack of an appropriate standard method for diet assessment in the African context.

Baseline characteristics of study respondents such as age, sex, prevalence of hypertension and diabetes also vary across the different studies and these are likely to affect the overall model performance in terms of discrimination and calibration which are affected by the distribution of risk factors included in the tested model and the baseline risk of diabetes in the study populations respectively. Interpretation of model performance will have to take into account the differences in these baseline characteristics.

Combining data from different countries is aimed at developing a risk score that could be applicable to a wider population. It also has the advantage of increasing the number of desired outcomes, hence provide an adequate sample for model derivation and reduce the risk of overfitting that occurs when a model is developed with inadequate sample. Heterogeneity in model performance of the new model will be assessed to account for the differences in background characteristics in the overall model performance.

Despite having the advantages of sample size, there are several limitations to the data. There is an overrepresentation of women in all the studies, so care needs to be taken in generalizing the study findings to other populations. There were also participants with missing values across countries, although few, because a complete case analysis was undertaken this could introduce bias in the model performance especially if the variable were not missing at random. Some variables were not at all present in some countries therefore not all risk scores will be able to be validated in all studies.

Chapter 6. Derivation and Internal Validation of a New Model

6.1 Introduction

Previous chapters highlighted the increasing prevalence of diabetes and the need for early identification of undiagnosed cases in order to implement disease-modifying intervention and prevent long-term complications. Recent developments in treatment and prevention of diabetes and cardiovascular complications present opportunities for screening of people at risk of diabetes. Availability of a simple reliable test is one of the requirements before a disease is considered for screening. Available tests for diabetes screening as described in the previous chapter include Oral Glucose Tolerance Test (OGTT), Fasting Glucose Test (FPG), Random Blood Glucose (RBG) Test Glycated Haemoglobin (HbA1c) and diabetes risk questionnaire (scores). Tests such as FPG, RBG, OGTT and HbA1c are invasive procedures and are costly and some tests such as OGTT have weak reproducibility (Barr et al., 2002), therefore making risk scores more convenient for use a first screening method in community settings.

Diabetes risk questionnaires and known diabetes risk factors have been used in predicting the presence of undiagnosed diabetes and have been reported to perform fairly well in identifying prevalent cases of diabetes and to improve the yield when used for screening in combination with other tests. A study in the Netherlands reported that risk stratification using a risk score before performing the biochemical measurements lowered significantly the number needed to screen to identify a case of diabetes, in this study, the number needed to screen was 233 in the low risk group versus 37 in the high risk group (Klein Woolthuis et al., 2009). Similarly a study in India showed that the India Diabetes Risk Score was able to identify up to 75% of diabetes cases diagnosed with OGTT, and a two-step screening alogarithm, comprising of the risk score as an initial test followed by OGTT was most cost effective (Mohan et al., 2011).

A considerable number of risk diabetes scores have been published (Noble et al., 2011). However, existing diabetes risk questionnaires/ models have mainly been developed and validated in White populations. Glummer and colleagues assessed the Rotterdam risk score in eight different ethnic populations including an African population from Cameroon (Glumer et al., 2006). The score had an AUC, Sensitivity and Specificity of

0.68 (95% CI, 0.64 to 0.72) 78% and 55% respectively in the developmental White population. In the African population the score had an AUC, Sensitivity and Specificity of 0.53 (95% CI, 0.48 to 0.71), 16.7% and 91% respectively. The poor performance observed in this study could be explained by possible interaction between ethnicity and the association of the predictor variables with the outcome. The aim of this study is to develop a risk score for undiagnosed diabetes applicable to populations in Africa. This chapter describes the process of derivation and internal validation of a new risk model to predict undiagnosed prevalent diabetes; Included in this chapter is the description of the methods, results and discussion.

6.2 Methods

6.2.1 Data

Data used for analysis is a pooled dataset comprising of data from diabetes survey in Tanzania, Guinea and Senegal (individual data sets are described in detail in (Chapter 5 on page 76). A total of 5193 cases excluding those with known diabetes were used for analysis, of these 327 (6.2%) had diabetes and 143 (2.7%) had undiagnosed diabetes , the low prevalence of undiagnosed diabetes could be because the data used in risk score derivation came recent studies that were conducted after the year 2000 and for example the study in Tanzania was conducted in an urban area which was a project site for the Adult Morbidity and Mortality Project where similar survey were conducted therefore majority of the community members were aware of their diabetes status, similarly this was a second diabetes survey for Guinea. The population for deriving the score was combined from 3 different countries to get a data set that is large enough to give adequate sample size and power. Applying the rule of thumb of 10 events per variable (Harrell Jr et al., 1996, Steyerberg et al., 2000) the sample is adequate for a model of up to 14 variables.

6.2.2 Outcome Variable

The outcome variable used in the analysis is presence of newly diagnosed diabetes. The outcome variable was defined as fasting blood glucose of >7mmol/l (WHO, 2006).

6.2.3 Candidate Variables

Variables considered for inclusion into the model were age, sex, body mass index (BMI), level of education(primary or less, secondary and tertiary), waist circumference, smoking (current or past smoker), and hypertension (history of hypertension, and or systolic blood

pressure of more or equal to 140 mmHg and or diastolic blood pressure of more or equal to 90 mmHg). In selecting variables for building the model the following criteria were used;

1) The variables are known risk factors for diabetes from published research findings.
2) Standard measurement procedures exists for example blood pressure, height, weight, waist circumference and education status.

6.2.4 Missing data

Data analysis was done using complete case analysis.

6.2.5 Model Development

Variable Selection

To develop the model a logistic regression model was fitted with the presence of diabetes modelled as a binary outcome, below is an outline of how the variables were selected for inclusion into the model.

Variable selection was done using backward stepwise selection method .The following steps were used in variable selection;

Step 1: Univariable analysis of each of the predictor variables was done to assess the relationship of the individual predictors to the outcome. This was done by studying the estimated coefficients resulting from fitting the model, and their significance compared to the null model.

Step 2: All predictor variables with a p value of 0.1 were entered together in a model. The cut-off point was chosen to ensure that it allows potentially important predictors in to the model. Following the fit of a multivariable model, the estimated coefficients and the p values of the predictor in the multivariable model were compared to those in the univariable analysis, non-significant predictors (p value > 0.1) were then eliminated at this stage and a new model with significant predictors was then fitted. Performance of the new fitted model was then compared with the full model; the process was repeated until the model contained only significant predictors. the decision to remove or keep these variables in the model was based on the changes in -2log likelihood ratio (-2LL) and where competing models had the same numbers of degrees of freedom the Akaike

Information Criteria was used to select the best model where the lower the value the better the model.

Step 3: To ensure that no significant predictor is left out on the basis of their significance at univariate analysis, variables excluded at that stage of analysis were then re-introduced and assessed for their effects on the model performance.

Step 4: After obtaining the preliminary model, the final variables were checked to make sure that no term included in the model can be omitted without significantly reducing the performance of the model, nor should there be any term that significantly improves model performance upon inclusion

Testing Interactions

After obtaining the preliminary model in step 3 above, interactions terms for age and predictors were added into the model. Variable interactions were therefore assessed by including specific interaction terms of the pre specified variables included in the model and assessing their effect on overall model performance. Similar cut of point of 0.1 for significance was applied for inclusion of interaction terms into the model. Significant interactions were then added into the model.

6.2.6 Assessing Model Assumptions

In order to derive an adequate model, the basic assumption of regression analysis namely the distribution of the outcome and linearity of the continuous predictors in the model have to be achieved, to assess whether the model developed fits this assumption, basic regression diagnostic tests were carried out (Frank E. Harell, 2001, Steyerberg, 2009).

Assessing Linearity

All continuous predictors were assessed for linearity. Linearity was assessed using residual plots, in which standardized deviance residuals from regression analysis of the variables were plotted against each of the predictor variables. An index plot of the standardized residuals were also made to assess whether the model fits the data well which is expected to show no particular pattern if the model is well fitted. In addition, transformations were done by application of restricted cubic splines (RCS) with 3-4 knots. Best model was then chosen based on the Akaike's Information Criterion (the lower the value the better the model).

Assessing overly influential variables

Assessment of overly influential variables was also done for the continuous variables by performing exploratory analysis of the variables such as using box plots and summary statistics to detect outliers and also by examining residuals and leverages after building the model. DFBETAS were used to examine the effects of the influential values on the model, using the DFBETA index plot. DFBETA for a particular observation is the difference between the regression coefficient calculated for all of the data and the regression coefficient calculated with the observation deleted. Assessment overly influential variables on the model was done by excluding individual cases with DFBETAS, residual and leverage values beyond the cut of points and running the model with the remaining cases, and comparing model performance with and without these cases.

6.2.7 Testing for Heterogeneity

Since data for developing the score was obtained from different settings/ countries meta-analysis of the resulting model performance measures (true negatives, false negatives, true positives and false positives at a uniform cut off point) from running the final model in country specific data was done. Analysis was performed using random effects model, heterogeneity was reported using the Cochrane (Q) and I^2 statistic (Higgins et al., 2003).

6.2.8 Assessing Model Performance

The performance of the model was assessed on 2 scales; calibration and discrimination(Frank E. Harell, 2001, Steyerberg, 2009). Discrimination is the overall ability to discriminate between those with and without undiagnosed diabetes in this case and calibration which is a measure of agreement between observed outcomes and the predicted probabilities

Discrimination

Model discrimination was measured using the Area under the Receiver Characteristics Curve (AUC). The AUC is the probability that a person with the outcome is assigned a higher probability of the outcome by the model, than a randomly chosen person without the outcome (Zweig and Campbell, 1993). A perfect model has a value of 1, therefore value closer to 1 depicts a better discrimination, a value of 0.5 shows no discrimination. In addition to assessing discrimination with AUC, assessment of improvement in overall discrimination of the model with additional variables was assessed using Integrated

Discrimination Improvement (IDI) and relative IDI. IDI was calculated as the difference in discrimination slopes between the baseline model and the model with additional variables, where discrimination slope is the difference in the mean predicted probabilities in those with and without events(Pencina, 2007). P value for IDI was calculated using the formula by Pencina (Pencina, 2007).

Calibration

Model calibration was assessed by the Hosmer Lemeshow test, a non-significant test depicts good calibration (Hosmer and Lemeshow, 2000, Moons et al., 2012). Calibration was also assessed visually by graphically plotting the observed outcome frequencies on the y axis against the mean predicted outcome probabilities on the x axis, within subgroups (deciles) of participants ranked by increased estimated probability and by plotting a bar graph of the estimated probabilities grouped by observed and predicted outcomes.

Yates slope was also used to assess calibration. Yates slope (discrimination slope) is the difference in the mean predicted probabilities among those with and without the outcome, in comparing models, the higher the value the better the model.

6.2.9 Internal Validation

Internal validation is the estimation of predictive accuracy of a model in the same population used to develop the model (Steyerberg et al., 2001). Internal validation was done using bootstrap procedure (Harrell Jr et al., 1996, Steyerberg, 2009). The validation was done using 1000 bootstrap resamples. 1000 bootstrap samples were drawn with replacement; the resampling was done by country to allow each sample to have exactly the same distribution of participants as in the original sample. A new model was constructed in each of the bootstrap sample and performance (AUC) assessed (bootstrap performance). The resulting bootstrap model was also applied into the original data set (test performance). Optimism was calculated as the difference between bootstrap performance and test performance, average optimism from the 100 bootstrap samples was used to calculate optimism corrected performance. Optimism corrected performance was obtained from subtracting optimism estimate from the model performance in the original data set.

6.2.10 The Point Scoring System

To make the model more practical for use in clinical settings, The regression (β) coefficients of predictors in the model were used to calculate weights for the point based scoring system, based on approach developed by Sullivan in the Framingham Heart Study (Sullivan et al., 2004). The continuous variables were first organized into categories and referent values were chosen. Referent values were set as the midpoint for the categories of continuous variables and base category was chosen, 1^{st} and 99^{th} percentile values were used to set mid points for the first and last categories. The next step was to determine the difference of each category referent value to the base category value in regression units. The risk associated with 5 year increase in age was set as the constant multiplier that reflects 1 point in the scoring system. Finally the point score was derived by dividing the difference obtained above by the set constant and the risk associated with each of the point totals were estimated. The risk associated with each of the point score was then estimated.

6.2.11 Cut off Point for the Score

In order to validate the developed score using the simple point score for the derived score, a cut off point was derived using *lsens* command in STATA, which plots sensitivity vs specificity for the possible cut offs for the score from which the cut off which maximised sensitivity and specificity was chosen.

6.3 Results

6.3.1 Model Building

The results of fitting univariable logistic regression to the model are shown in

Table 6-1. For categorical variables, the following were modelled as referent values; Sex, Male; Hypertension, No Hypertension; Education Level, less than primary school and Smoking, Non Smoker. In univariable analysis, significant predictors of undiagnosed prevalent diabetes were: BMI, Age, Hypertension and Waist circumference and smoking.

At multivariable analysis significant variables (p value < 0.05) were age, hypertension, waist circumference and smoking, after removing BMI and education level smoking was no longer a significant predictor (p value > 0.05) Table 6-2. Introduction of the non-significant variables at univariate analysis, namely education level and sex did not improve the model performance; therefore none of these predictors were left in the model.

Table 6-1 Results of Fitting Univariable Logistic Model

Variable	Odds Ratio (95% CI)	Coefficient	Std. Err	p Value
Age	1.06 (1.05 to 1.07)	0.061	0.008	<0.001
Waist	1.06 (1.05 to 1.07)	0.058	0.007	<0.001
BMI	1.09 (1.07 to 1.13)	0.095	0.013	<0.001
Sex (Female)	1.24 (0.76 to 2.04)	0.218	0.253	0.39
Hypertension (Yes)	4.2 (2.58 to 6.93)	1.440	0.253	<0.001
Level of Education				
Primary	0.74 (0.39 to 1.35)	-0.307	0.311	0.32
Secondary	0.96 (0.51 to 1.78)	-0.043	0.318	0.89
Tertiary	1.09 (0.48 to 2.51)	0.090	0.423	0.83
Smoking (Yes)	2.21 (0.96 to 5.13)	0.796	0.953	0.06

CI= Confidence Interval, Std. Err = Standard Error of Coefficients

Table 6-2 Results of Fitting a Multivariable Logistic Model

Variable	Odds Ratio (95% CI)	Coefficient	Std. Err.	Pvalue
Smoking (Yes)	2.37 (0.95 to 5.86)	0.862	1.090	0.06
Waist	1.04 (1.02 to 1.06)	0.037	0.010	<0.001
Age	1.05 (1.03 to 1.07)	0.049	0.010	<0.001
Sex (Female)	0.67 (0.36 to 1.23)	-0.394	0.207	0.20
BMI	1.04 (0.98 to 1.08)	0.034	0.025	0.16
Education Level				
Primary	0.91 (0.48 to 1.73)	-0.090	0.299	0.78
Secondary	1.70 (0.80 to 3.38)	0.532	0.594	0.13
Tertiary	1.12 (1.09 to 3.21)	0.110	0.510	0.81
Hypertension (Yes)	1.88 (1.12 to 3.13)	0.630	0.512	0.02

-2Loglikelihood= -304.14 Pseudo R^2 = 0.159

Table 6-3 below shows results of the preliminary model after fitting the significant predictors into a multivariable model. The fitted model resulted into a model with AIC of 625.745 (4 degrees of freedom) and Nagelkerke's R^2 of 0.148.

Table 6-3 Regression Coefficients (95% CI) and Standard Error of Predictors in the Preliminary Model

Variable	Odds Ratio (95% CI)	Coefficient (SE)	pValue
Age (per 1 year increase)	1.05 (1.02 to 1.07)	0.045 (0.009)	<0.001
Waist Circumference (per cm increase)	1.05 (1.03 to 1.06)	0.048 (0.007)	<0.001
Hypertension (present)	1.92 (1.12 to 3.26)	0.649 (0.271)	0.017
Intercept		-11.012(0.811)	<0.001

-2Log likelihood = -308.87, Pseudo R^2 = 0.148, SE = Standard Error

After obtaining the preliminary model, interaction terms for BMI*age, waist circumference*age, and hypertension*age were tested. At univariate analysis, interaction terms for waist circumference, BMI were significant and were further tested for inclusion into the model.

When the interaction terms were added in the model none of the variables were significant, p value > 0.05. To assess whether the model contain all the significant variables at univariate analysis including BMI, interaction terms BMI*age and waist circumference*age were each added into the model and its effect of adding in to the model were assessed in terms of improvement in risk stratification.

Highest improvement in risk stratification was achieved on adding BMI, age interaction for BMI and waist circumference (signifying that older subjects are more likely to have higher waist circumference and higher BMI by virtue of their age) (Table 6-4). However the overall improvement was non-significant.

Table 6-4 Assessment of Improvement in Risk Stratification with Additional Variable in the Model

Model	df	-2LL	AIC	IDI	P val	rIDI (%)
Age, Waist and Hypertension	4	-308.87	625.75	-	-	-
Age, Waist, Hypertension and BMI	5	-307.93	625.85	0.0013	0.93	3.93
Age, Waist, Hypertension , BMI and Age*BMI	6	-307.93	625.85	0.0011	0.91	3.54
Age, Waist , Hypertension and Age*Waist	5	-308.87	627.74	0.0006	0.97	1.73

Key
rIDI = Relative Integrated Discrimination Improvement
IDI = Integrated Discrimination Improvement
AIC = Akaike Information Criteria
Df = Degrees of Freedom
P Val = P Value
BMI = Body Mass Index

Assessment of Model Fit

Assessment of overly influential variables was done using DFBETAs and leverage using index plots, regression analysis was done with and without the influential variables, there were no model improvement after excluding the influential variables. All the variables were then kept in the model.

As mentioned in the methods, linearity assumptions were assessed using residual plots such as index plot of the residuals and plots of residuals and the continuous variables in the model. Results showed that the model fulfils the basic assumptions of linearity. Below, shows a plot of residuals vs. age and waist circumference. The plots do not show any particular pattern.

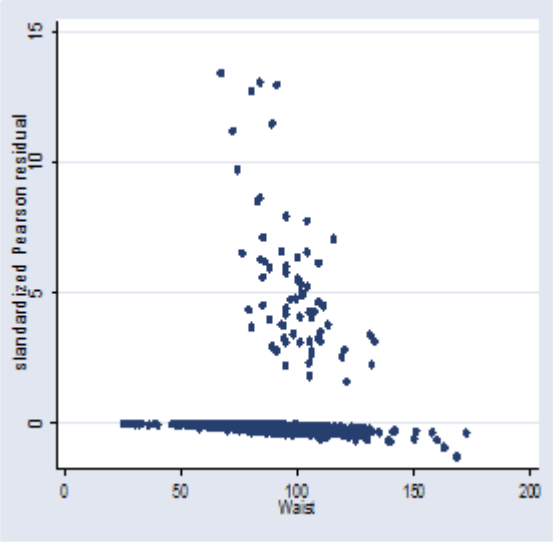

Figure 6-1 Residual plot for Waist Circumference

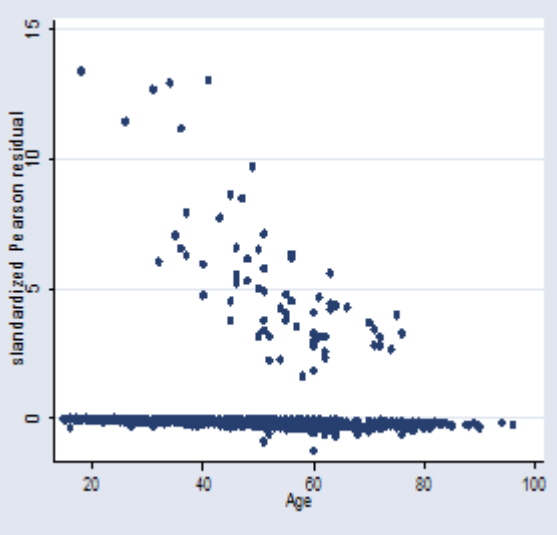

Figure 6-2 Residual Plot for Age

To test linearity assumptions further the model was fitted as linear and also fitted continuous variables as restricted cubic splines with 3 and 4 knots and compared with the linear model results of which are presented in Table 6-5 below. Results show that for age the model has best performance when age was modelled as linear. However, for waist circumference the performance slightly improved when waist circumference was modelled with 3 knots showing that the distribution of waist circumference measures may be less linear. Waist circumference was not log transformed or modelled with knots because there was not much difference in the performance when modelled as linear vs with knots, with the aim to keep the model simple.

Table 6-5 Age and Waist Modelled With Restricted Cubic Splines

Model	Position of knots	Df	-2LL	AIC
Age				
None		3	-320.108	646.2
Linear		4	-308.873	625.8
RCS 3 knots	20, 37 and 59	5	-307.960	625.9
RCS 4 knots	17, 30, 45 and 63	6	-308.009	628.1
Waist Circumference				
None		3	-328.284	662.6
Linear		4	-308.873	625.8
RCS 3 knots	68, 82, 100	5	-307.207	624.4
RCS 4 knots	65, 77, 88, 107	6	-306.424	624.8

Key
RCS = Restricted Cubic Splines
Df = Degrees of Freedom
-2LL = -2 Log Likelihood
AIC = Akaike Information Criterion

6.3.2 Final Model

Assessment of new variables for inclusion in the model did not yield significant results, the model presented in Table is chosen as the final model. The probability of undiagnosed diabetes using the model is given by;

$$P = \exp x \; / \; 1+\exp x$$

Where $x = [(-11.012 + 0.045(Age) + 0.048\ (Waist\ Circumference) + 0.649\ (Hypertension)]$

6.3.3 Apparent Model Performance

Discrimination

The performance of the developed model in predicting undiagnosed diabetes is shown in Figure 6-3 below. The Area under the ROC curve for the model is 0.83 (95% CI 0.82 to 0.84).

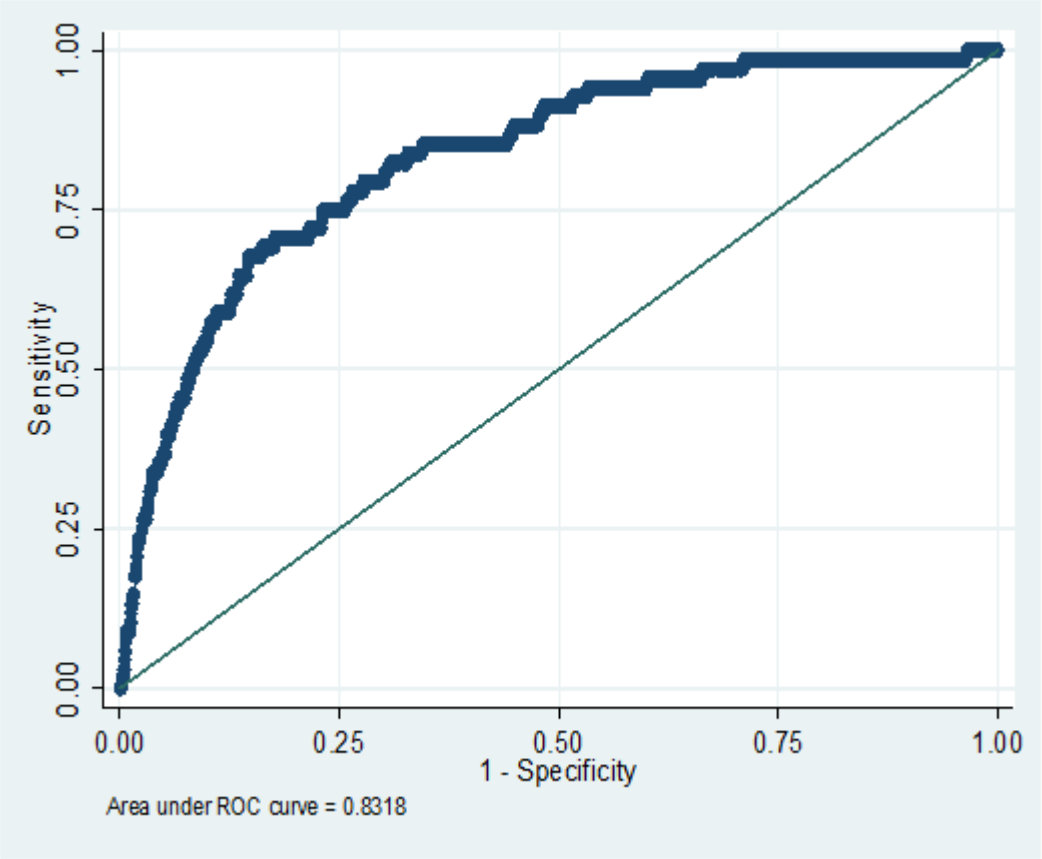

Figure 6-3 ROC Curve for the Model in the Development Data Set

Calibration

Below, (Figure 6-4) is a calibration graph showing the agreement between the observed outcomes and predictions, over a range of predicted probabilities. The graph shows increased proportion with observed outcomes with increasing predicted probabilities. The final model has a non-significant Hosmer-Lemeshow statistic (Hosmer and Lemeshow, 2000) with a p value 1.0, showing that the model has good calibration and a Yates slope of 0.03.

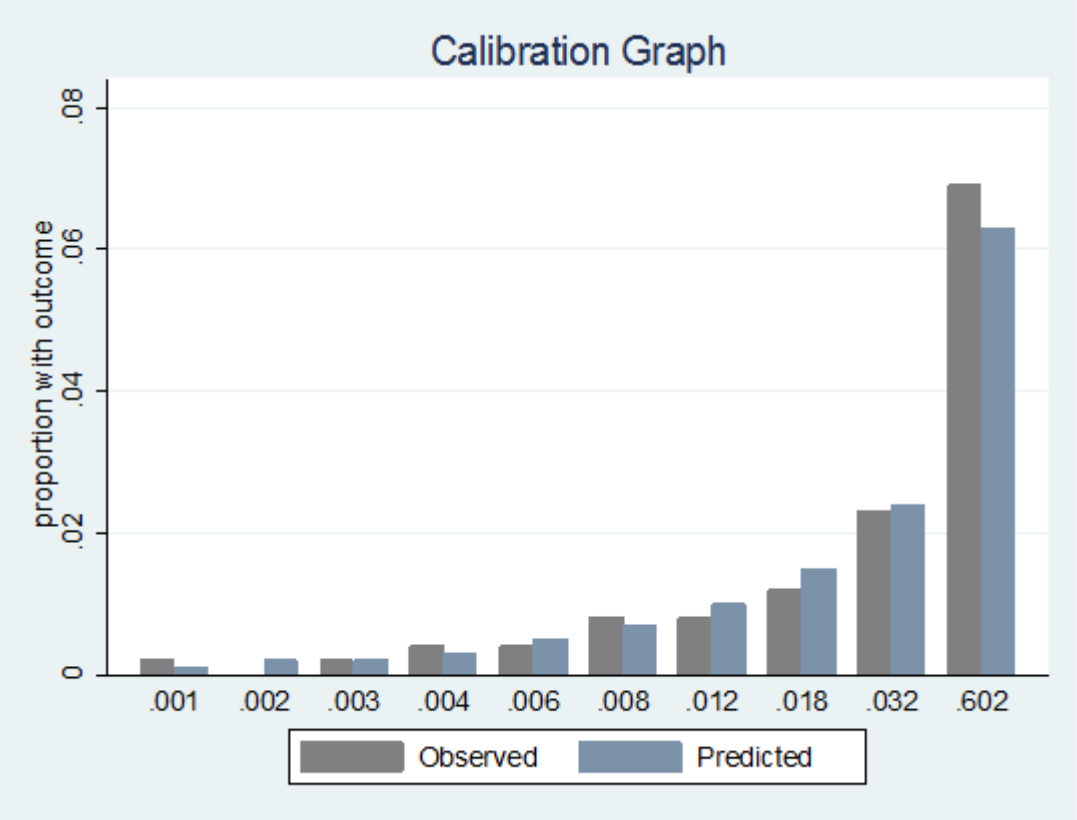

Figure 6-4 Calibration Graph of Observed Outcome and Predictions vs. Predicted Probabilities

Key
H-L = Hos
X^2 = Chi s

Yates Slope: 0.03
H-L χ^2: p value 1.0

6.3.4 Fitting the Model in Country Specific Data and Meta-Analysis

Meta-analysis of the results of fitting the model in the country specific populations, presented in Figure 6-5 below yielded an AUC of 0.8 and a Cochrane (Q) statistic of 0.7 with a resulting I^2 of 0.

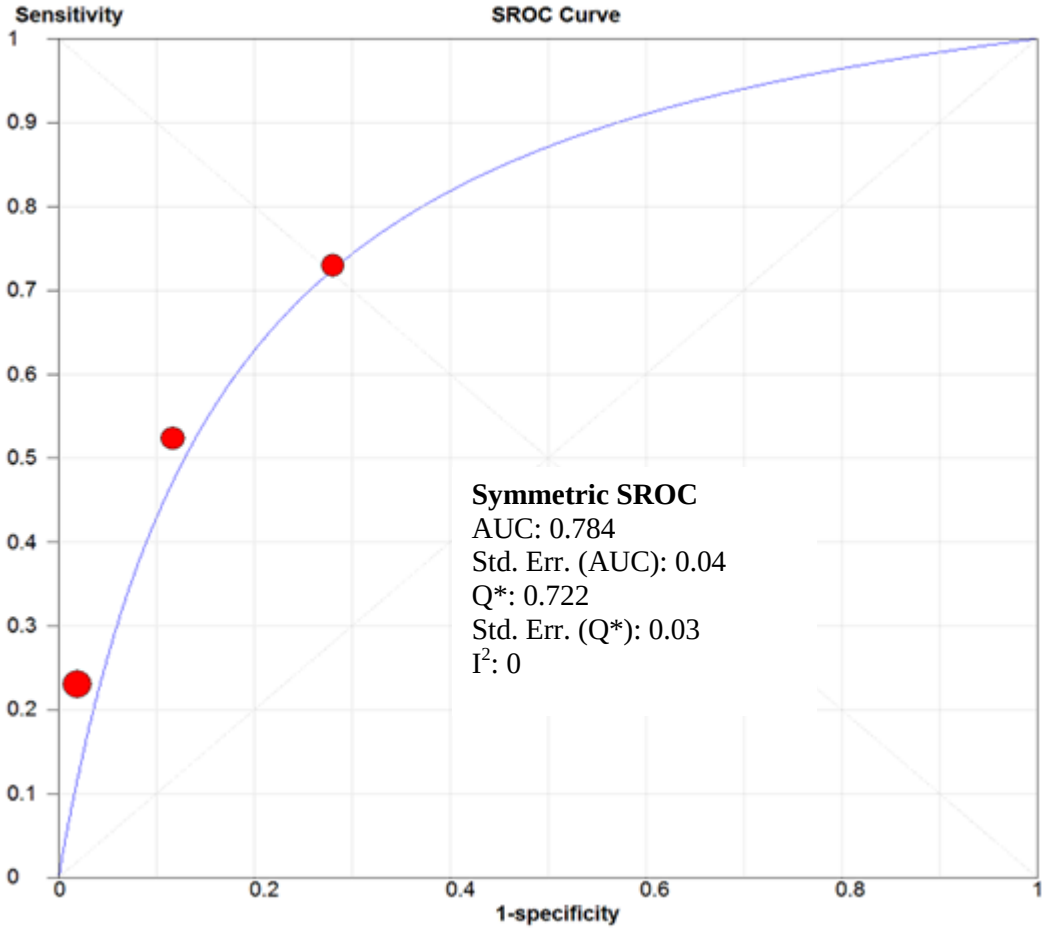

Figure 6-5 Summary ROC Curve for Applying the Model in Country Specific Data

Key
SROC = Summary Receiver Operating Characteristic Curve
AUC = Area under the Curve
Std. Err. = Standard Error
Q = Qochrane Statistic
I^2 = Inconsistency score

6.3.5 Point Scoring System

To make the model applicable to a clinical setting, the final model was transcribed into a simple point score integer; development of the score points is described in detail in the methods in page 111. Table 6-6 below shows the point score for each of the variable categories. The total score ranges from -9 which is the lowest risk category to 15 which is the highest risk category. Table 6-7 shows the risk function corresponding to the absolute risk function corresponding to the risk score totals. The best cut off point for the score was ≥7 point totals.

Table 6-6 Simple Scoring System Based on the Final Model

Risk factor	Categories	Reference Value	β	B (Value-Referent)	Points
Age			0.045		
	<30	22.50		-0.540	-2
	30-39	34.50*		0.000	0
	40-49	44.50		0.450	2
	50-59	54.50		0.900	4
	>60	67.50		1.485	7
			0.048		
Waist	<80	52.50		-1.560	-7
	80-90	85.00*		0.000	0
	90-100	95.00		0.480	2
	>100	110.00		1.200	5
			0.649		
Hypertension	No	0.00*		0	0
	Yes	1		0.649	3

Key
**Referent value*
β = Regression Coefficient

Table 6-7 Total Points, Absolute and Percentage Risk Function For Undiagnosed Diabetes for Each of the Total Score Points

Points Total	Absolute Risk	Percentage Risk
-9	0.00	0.00
-8	0.00	0.00
-7	0.00	0.00
-6	0.00	0.00
-5	0.00	0.00
-4	0.00	0.00
-3	0.00	0.00
-2	0.00	0.00
-1	0.00	0.00
0	0.00	0.46
1	0.01	1.24
2	0.03	3.29
3	0.08	8.47
4	0.20	20.11
5	0.41	40.62
6	0.65	65.03
7	0.83	83.49
8	0.93	93.22
9	0.97	97.39
10	0.99	99.02
11	1.00	99.64
12	1.00	99.87
13	1.00	99.95
14	1.00	99.98
15	1.00	99.99

Distribution of the Total Score Points in Validation Studies

Distributions of the total score points in the different validation study populations are presented in Table 6-8, Table 6-9, Table 6-10 and Table 6-11 below. Results show that compared to the percentage risk functions presented in Table 6-7 above the risk score performs well in excluding those that do not have diabetes except in the Guinea population (Table 6-10) , but overall it overestimates risk in those with high risk score totals. The percentage of those with outcome (diabetes) is small therefore the results need to be interpreted with caution.

Table 6-8 Distribution of Total Score by Diabetes Status in the CRIBSA Validation Study Population

Total Score Points	Without Diabetes			With Diabetes		
	Frequency	Percent	Cumulative Percent	Frequency	Percent	Cumulative Percent
-9	70	6.74	6.74	0	0.00	0.00
-7	62	5.97	12.72	0	0.00	0.00
-6	7	0.67	13.39	0	0.00	0.00
-5	26	2.50	15.90	0	0.00	0.00
-4	19	1.83	17.73	0	0.00	0.00
-3	9	0.87	18.59	0	0.00	0.00
-2	48	4.62	23.22	0	0.00	0.00
0	107	10.31	33.53	2	5.00	5.00
1	7	0.67	34.20	0	0.00	0.00
2	61	5.88	40.08	0	0.00	0.00
3	61	5.88	45.95	0	0.00	0.00
4	45	4.34	50.29	2	5.00	10.00
5	81	7.80	58.09	2	5.00	15.00
6	20	1.93	60.02	1	2.50	17.50
7	109	10.50	70.52	4	10.00	27.50
8	33	3.18	73.70	3	7.50	35.00
9	53	5.11	78.81	6	15.00	50.00
10	63	6.07	84.87	2	5.00	55.00
12	108	10.40	95.28	10	25.00	80.00
15	49	4.72	100.0	8	20.00	100.00
	1,038	100.0		40	100.00	

Table 6-9 Distribution of Total Score by Diabetes Status in the KZN Validation Study Population

Total Score Points	Without Diabetes			With Diabetes		
	Frequency	Percent	Cumulative Percent	Frequency	Percent	Cumulative Percent
-9	115	13.96	13.96	0	0.00	0.00
-7	42	5.1	19.05	0	0.00	0.00
-6	12	1.46	20.51	0	0.00	0.00
-5	32	3.88	24.39	0	0.00	0.00
-4	8	0.97	25.36	0	0.00	0.00
-3	16	1.94	27.31	0	0.00	0.00
-2	44	5.34	32.65	1	2.56	2.56
0	95	11.53	44.17	4	10.26	12.82
1	6	0.73	44.9	0	0.00	0.00
2	38	4.61	49.51	2	5.13	17.95
3	66	8.01	57.52	2	5.13	23.08
4	33	4	61.53	0	0.00	0.00
5	31	3.76	65.29	3	7.69	30.77
6	15	1.82	67.11	1	2.56	33.33
7	72	8.74	75.85	6	15.38	48.72
8	5	0.61	76.46	0	0.00	0.00
9	37	4.49	80.95	3	7.69	56.41
10	58	7.04	87.99	4	10.26	66.67
12	62	7.52	95.51	7	17.95	84.62
15	37	4.49	100	6	15.38	100.00
Total	824	100		39	100	

Table 6-10 Distribution of Total Score by Diabetes Status in the Guinea Validation Study Population

Total score Points	Without Diabetes			With Diabetes		
	Frequency	Percent	Cumulative Percent	Frequency	Percent	Cumulative Percent
-7	363	25.16	25.16	8	12.12	12.12
-5	180	12.47	37.63	4	6.06	18.18
-4	27	1.87	39.5	0	0.00	0.00
-3	130	9.01	48.51	2	3.03	21.21
-2	45	3.12	51.63	1	1.52	22.73
0	178	12.34	63.96	6	9.09	31.82
2	50	3.47	67.43	1	1.52	33.33
3	94	6.51	73.94	12	18.18	51.52
4	65	4.5	78.45	1	1.52	53.03
5	37	2.56	81.01	1	1.52	54.55
6	19	1.32	82.33	0	0.00	0.00
7	85	5.89	88.22	5	7.58	62.12
8	1	0.07	88.29	1	1.52	63.64
9	45	3.12	91.41	9	13.64	77.27
10	50	3.47	94.87	7	10.61	87.88
12	59	4.09	98.96	6	9.09	96.97
15	15	1.04	100.00	2	3.03	100.00
Total	1,443	100.00		66	100.00	

Table 6-11 Distribution of Total Score by Diabetes Status in the Tanzania Validation Study Population

Total Score Points	Without Diabetes			With Diabetes		
	Frequency	Percent	Cumulative Percent	Frequency	Percent	Cumulative Percent
-9	29	3.29	3.29	0	0.00	0.00
-7	57	6.47	9.76	0	0.00	0.00
-6	1	0.11	9.88	0	0.00	0.00
-5	25	2.84	12.71	0	0.00	0.00
-4	9	1.02	13.73	0	0.00	0.00
-3	18	2.04	15.78	1	1.01	1.01
-2	19	2.16	17.93	0	0.00	0.00
0	68	7.72	25.65	4	4.04	5.05
1	4	0.45	26.11	0	0.00	0.00
2	88	9.99	36.10	8	8.08	13.13
3	28	3.18	39.27	5	5.05	18.18
4	70	7.95	47.22	2	2.02	20.2
5	67	7.60	54.82	7	7.07	27.27
6	28	3.18	58.00	3	3.03	30.3
7	87	9.88	67.88	11	11.11	41.41
8	17	1.93	69.81	7	7.07	48.48
9	56	6.36	76.16	13	13.13	61.62
10	64	7.26	83.43	11	11.11	72.73
12	100	11.35	94.78	21	21.21	93.94
15	46	5.22	100.00	6	6.06	100.00
Total	881	100		99	100.00	

6.3.6 Model Validation

The model was internally validated using bootstrap procedure. The average optimism from the model was 0.03; therefore the optimism corrected performance (AUC) for the model is 0.8.

6.4 Discussion

To my knowledge this is the first study in Africa to describe the development of a diabetes risk score to detect prevalent diabetes. Recent developments in diabetes prevention and treatment have resulted in strong arguments in favour of opportunistic diabetes screening (Echouffo-Tcheugui et al., 2011, Echouffo-Tcheugui et al., 2012). For any screening programme to be effective there is need for feasible, reliable and cost effective screening methods. Several risk scores have been developed to screen for undiagnosed diabetes as described in chapter 3, mostly in White populations and these scores have poor performance when applied to other ethnic populations.

This study focused on developing a risk score for detecting prevalent diabetes for use as an initial screening tool for undiagnosed diabetes. The score uses risk factors known to be associated with diabetes to predict prevalent diabetes. Risk factors included in this score are hypertension, age and waist circumference, which have been widely used in other diabetes risk scores. The presence of hypertension contributed more points towards risk prediction compared to other variables tested for model development.

Body mass index was not a significant predictor in this model; waist circumference had better performance and was chosen for inclusion in the model. The reason why BMI was not a good predictor of diabetes could be due to the fact that the overall obesity measured by BMI does not necessarily corellate with the level of visceral fat. A study looking at ethnic differences in the incidence of diabetes found that BMI was less correlated with diabetes for the Africans compared to the Asians and White populations (Shai et al., 2006), and possibly the appropriate cut off points to define risk are different for different ethnic groups. Studies have suggested that waist circumference could be a better predictor of diabetes risk than BMI which seem to support the findings in this study (The InterAct, 2012, Chan et al., 2003). IDF recommends different cut-off points for waist circumference (IDF, 2006) with lower cut off points for Asian population and no specific cut points for the African population because of lack of data. In this study no categorization of data was done all continuous data was modelled as linear.

Risk factors, such as diet and physical activity, were not considered for inclusion into the model because of the lack of standardized methods for measurements in this particular

population and also the need to have a simple score with covariates that can be consistently measured across different settings.

Family history of diabetes was also not considered because of the lack of the variable in the data sets, it is an important risk factor for diabetes however information on parent or sibling diabetes status is likely to be incomplete given the high prevalence of undiagnosed cases in the African population that could be due to limited diagnostic facilities and poor access to health care.

The risk score presents a feasible approach for diabetes screening with good discrimination (AUC 0.83), identifying individuals at high risk that should be referred for further diagnostic tests. The score points have been transformed into simple integer points that can easily be computed. For the derivation study the best cut off point for the score was ≥ 7 which was chosen to maximise both sensitivity and specifity for the purpose of evaluating the performance of the score in this study. In clinical decision making the choice of the best cut off point is a complex one and there is no universal cut off point that is applicable to all, the choice should be guided by the aim of the screening program, the resources available and the weighted cost of false positive and false negative results.

What is unique about this study is that data used to develop the score were obtained from 3 different countries in an attempt to make the score applicable to a wider African population and also to take advantage of a larger sample size. A meta-analysis of the score applied in country specific data showed that the performance of the score was homogenous in the 3 countries.

The study limitations included that fact that cross sectional data was used to develop the score and diabetes diagnosis was made based on a single fasting glucose using point of care devices in all the 3 studies, therefore the true diabetes prevalence could have been underestimated. Also the data used for score derivation, was obtained from different studies in different countries therefore may be a source of bias due to heterogeneity of the studies.

In conclusion the derived tool is a potential screening tool for detection of prevalent diabetes in African populations. However measuring waist circumference appropriately could be a challenge in the application of this risk score in practice and would limit its applicability as a self-assessment score. Examples of the approaches will be to use the score at the health facility level for opportunistic screening of individuals attending for

other ailments or during community outreach programs by the public health nurses, but the challenges remain with how the data will be collected, who is responsible for evaluating the program and also the resources needed for screening. More studies are needed to study the feasibility of using this score in practice and to test its acceptability also more studies are needed to validate the score and test performance in other African populations. The next chapters will look at external validation of the new model and subsequent comparison of the model to a selection of existing diabetes risk scores.

Chapter 7. External Validation and Comparison of Performance of the New Model to Existing Models

7.1 Introduction

Previous chapters described the derivation and internal validation of a new diabetes risk score for African populations. The aim of developing the new model was to derive a diabetes score that would be applicable with good performance across different populations within Africa. The aim of this part of the study described in this chapter is to compare the performance of the new tool to independent populations, to test the generalizability of the model to other African settings. Existing models for predicting prevalent diabetes are also validated and performance compared to the new model. Only simple models without biochemical tests are included for validation. This chapter details the methods, results of external validation of the new model to the new populations and a comparison of the performance with existing diabetes risk scores from other settings.

7.2 Methods

7.2.1 Study Populations

To externally validate the score, the score was applied to populations form two studies in South Africa; from Cape Town (CRIBSA study) and the Kwazulu Natal study, and Guinea. The validation study populations are described in detail in Chapter 6 on page 76.

7.2.2 Identification of Prediction Models for Validation

Diabetes risk scores for validation were obtained by performing a keyword search in Medline and Embase as described in chapter three on Diabetes Risk Scores. Included are the risk scores to predict undiagnosed diabetes, that do not require laboratory testing. The simplified scores were used for model validation because the aim is to validate the new score in the form that would actually be applied in practice.

7.2.3 Assessment of Model Performance

The new score was applied to the validation data score by generating a score for each individual by using simplified score (Table 6-6). For the existing score, the score points were generated for each individual using the published score points as shown in Table 7-1. Original published score cut off points were used in the analysis. The cut off used for

the scores were ≥ 7 for the new score, ≥ 14 for the Chinese score (Gao et al., 2010), ≥ 10 for the Oman score (Al-Lawati and Tuomilehto, 2007), ≥ 18 for the Brazil score (Pires de Sousa et al., 2009), ≥ 21 (Ramachandran et al., 2005) and ≥ 16 (Chaturvedi et al., 2008) for the Indian scores, ≥ 5 for the US score (Bang et al., 2009) and ≥ 6 for the Rotterdam score (Baan et al., 1999).

Model performance was assessed by the Area under the Receiver Operating Characteristic curve (AUC), sensitivity and specificity. Sensitivity is defined as proportion of individuals with diabetes among those identified positive by the score and specificity is the proportion of individuals who truly do not have diabetes among those identified as negative by the score.

7.3 Results

7.3.1 Risk Scores for Validation

Below are the risk scores for predicting prevalent undiagnosed diabetes that were obtained from the search (Al Khalaf et al., 2010, Al-Lawati and Tuomilehto, 2007, Baan et al., 1999, Bang et al., 2009, Chaturvedi et al., 2008, Glümer et al., 2004, Keesukphan et al., 2007, Pires de Sousa et al., 2009, Ramachandran et al., 2005, Ruige et al., 1997, Tabaei and Herman, 2002, Gao et al., 2010). Of the remaining scores, 5 scores were not validated due to lack of suitable variables in the data sets (Al Khalaf et al., 2010, Glümer et al., 2004, Keesukphan et al., 2007, Mohan et al., 2005, Ruige et al., 1997). For example the Kuwait risk score (Al Khalaf et al., 2010) , the simplified Indian diabetes risk score (Mohan et al., 2005) and the Danish risk score (Glümer et al., 2004), could not be validated due to missing variables on history of diabetes in siblings or parents.

In the validation data history of diabetes was ascertained among first degree relatives and was not specified as sibling, mother or father. The Dutch symptom based risk score could not be validated because many of its variables were lacking in the data (Ruige et al., 1997). A total of 7 existing models (Al-Lawati and Tuomilehto, 2007, Baan et al., 1999, Bang et al., 2009, Chaturvedi et al., 2008, Ramachandran et al., 2005, Gao et al., 2010, Pires de Sousa et al., 2009) and the new model were validated in the South African populations and only 2 models ; the new model and the Brazil diabetes risk score (Pires de Sousa et al., 2009) were validated in the Guinea population due to lack of data.

Table 7-1 below shows a summary of the risk scores that were validated and a summary of how the variables were imputed. Almost all the required variables were present in the CRIBSA and KZN data sets to validate the models outlined in the table, except for use of hypertensive medication for the Dutch model (Baan et al., 1999) where history of hypertension was used as a proxy variable in validating this model in the data. Due to small number of undiagnosed cases in the CRIBSA and KZN validation data sets, no subgroup analyses were performed. In the Guinea data however the total events per variable permitted subgroup analysis and results were presented as both overall and by sex subgroups.

Table 7-1 Variable in Validated Models and Availability of Variables in Validation Data

Model	Variable	Variable definition in Model	CRIBSA	KZN	Guinea	Score
Chinese Risk Score (Gao et al., 2010)	Waist (Chinese chi≈33cm)	Men				
		≤ 2.3 chi	Yes	Yes	Yes	1
		2.4-2.6 chi				4
		2.7-2.9 chi				8
		≥3 chi				12
		Women				
		≤ 2.0chi				1
		2.1-2.3chi				3
		2.4-2.6 chi				6
		≥2.7chi				9
	Age (years)	≤35yrs	Yes	Yes	Yes	1
		36-45yrs				3
		46-55yrs				6
		56-65yrs				9
		≥65yrs				12
	Family history of diabetes	Yes	Yes	Yes	No	8
		No				1
Rotterdam Risk Score (Gao et al., 2010)	Age (years)	Age per 5 year increment form 55 years	Yes	Yes	Yes	2
	Sex	0, female; 1 male	Yes	Yes	Yes	5
	Use of antihypertensive medication	0, no; 1, yes	Proxy variable previous history of hypertension	Proxy variable previous history of hypertension	No	4

Model	Variable	Variable definition in Model	CRIBSA	KZN	Guinea	Score
	Obesity (BMI>=30kg/m2) both sex)	0, no; 1 yes	Yes	Yes	Yes	5
India Risk Score (Chaturvedi et al., 2008)	Age (years)	<40yrs	Yes	Yes	Yes	0
		40-49yrs				4
		>49yrs				6
	Blood Pressure (mmHg)	Optimal blood pressure (Systolic <120mmHg and Diastolic <80mmHg)	Yes	Yes	Yes	0
		Pre-Hypertension (Systolic 120-139mmHg and Diastolic 80-89mmHg)				5
		Hypertension (Systolic ≥ 140 mmHg or Diastolic ≥90 mmHg)				7
	Waist Circumference (cm)	Waist circumference ≤75cm (women) and ≤80 (men)	Yes	Yes	Yes	0
		Waist circumference >75cm but ≤85cm (women) and >80cm(men) but ≤90cm				9
		Waist circumference >85cm (women) and ≤90cm (men)				12
	Family history of diabetes	No	Yes	Yes	No	0
		Yes				4
India Risk Score, (Ramachandran et al., 2005)	Age (years)	<30yrs	Yes	Yes	Yes	0
		30-44yrs				10
		45-59				18
		>59				19
	Family history of diabetes	No	Yes	Yes	No	0
		Yes				7
	BMI (kg/m2)	<25kg/m2	Yes	Yes	Yes	0
		≥25kg/m2				7
	Waist circumference (cm)	<85cm (men), <80cm (women)	Yes	Yes	Yes	0

Model	Variable	Variable definition in Model	CRIBSA	KZN	Guinea	Score
		≥85cm (men), ≥80cm (women)				5
	Physical activity	Sedentary and light physical activity	Yes	Yes	No	4
Brazil risk score (Pires de Sousa et al., 2009)	Age (years)	35-44yrs	Yes	Yes	Yes	0
		45-54yrs				7
		>55				12
	BMI (kg/m2)	<25kg/m2	Yes	Yes	Yes	0
		≥25kg/m2 but >30 kg/m2				5
		≥30kg/m2				18
	Hypertension (Systolic BP≥140mmHg and or Diastolic BP ≥90 mmHg or use of hypertension medication)	No	Yes	Yes	Yes	0
		Yes				6
US Risk Score, (Bang et al., 2009)	Age (years)	≤40yrs	Yes	Yes	Yes	0
		40-49yrs				1
		50-59yrs				2
		≥60yrs				3
	Sex	Female	Yes	Yes	Yes	0
		Male				1
	Family history of diabetes	No	Yes	Yes	Yes	0
		Yes				1
	History of hypertension	No	Yes	Yes	No	0
		Yes				1
	Obesity (defined by both BMI (kg/m2) and Waist Circumference (inch)	Not overweight or Obese (BMI<25 and Waist circumference <37in (men), <31.5in (women)	Yes	Yes	Yes	0
		Overweight (BMI≥25 but <30 or waist circumference ≥37in but <40(men), ≥31.5in but <35(women)				1
		Obese (BMI≥30 but <40 or waist circumference				2

Model	Variable	Variable definition in Model	CRIBSA	KZN	Guinea	Score
		≥40in but <50(men), ≥35in but <49(women) Extremely Obese (BMI ≥40 or waist circumference ≥50(men), ≥49in(women)				3
	Physical activity	No	Yes	Yes	No	0
		Yes				-1
Oman Risk Score (Al-Lawati and Tuomilehto, 2007)	Age (years)	20-39yrs;	Yes	Yes	Yes	0
		40-59yrs;				7
		≥60yrs				9
	Waist Circumference (cm)	Men< 94cm, Women <80cm;	Yes	Yes	Yes	0
		Men ≥94cm, Women ≥80cm				2
	Body Mass Index (kg/m2	< 25kg/m2	Yes	Yes	Yes	0
		25-30kg/m2				2
		≥30kg/m2				3
	Family history of diabetes	0, no; 1 yes	Yes	Yes	No	8
	Current hypertension status (Systolic BP≥140mmHg and or Diastolic BP ≥90 mmHg)	0, no; 1 yes	Yes	Yes	Yes	3

Key
BMI = Body Mass Index

7.3.2 New Model Performance in Validation Populations

Performance of the newly developed risk score is presented below. The score had on overall performance in all the validation population with AUC ranging from 0.70 (95% CI 0.70 to 0.75) (Figure 7-5) in the Guinea validation population with lowest performance to 0.82 (95% CI 0.76 to 0.87) in the Cape Town study population (Figure 7-1). Also the overall performance was better when diabetes was defined using fasting glucose than when using OGTT, AUC in CRIBSA data were 0.82 (95% CI 0.76 to 0.87) versus 0.75 (95% CI 0.56 to 0.82) respectively see Figure 7-1 and Figure 7-2 below but the difference is not statistically significant.

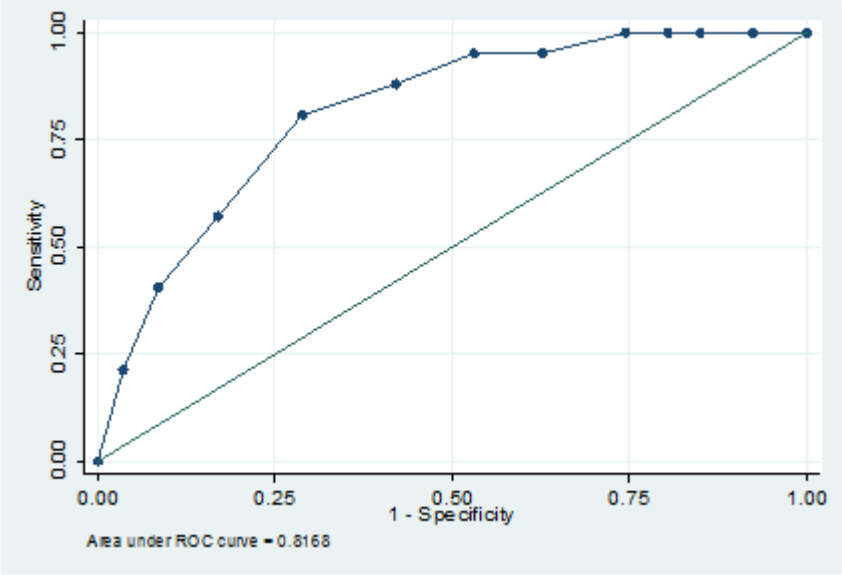

Figure 7-1 Model Performance in CRIBSA Data Diagnosis by Fasting Glucose

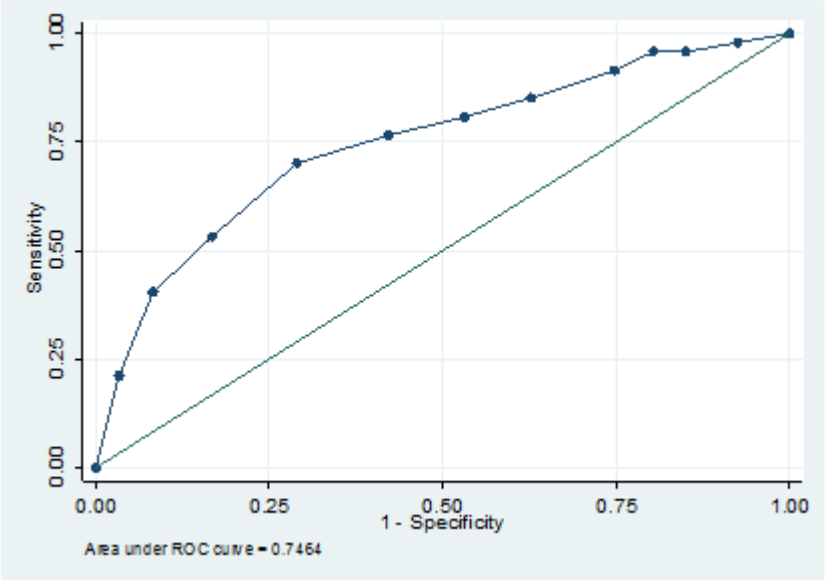

Figure 7-2 Model Performance in CRIBSA Diabetes Diagnosis by OGTT

When the new score was validated in a rural black South African population in the KZN data the score performance in terms of the Area under the ROC curve ranged from 0.70 (95% CI 0.62 to 0.78) to 0.8 (95% CI 0.77 to 0.83) using OGTT and fasting glucose respectively signifying good ability to discriminate between cases and non-cases.

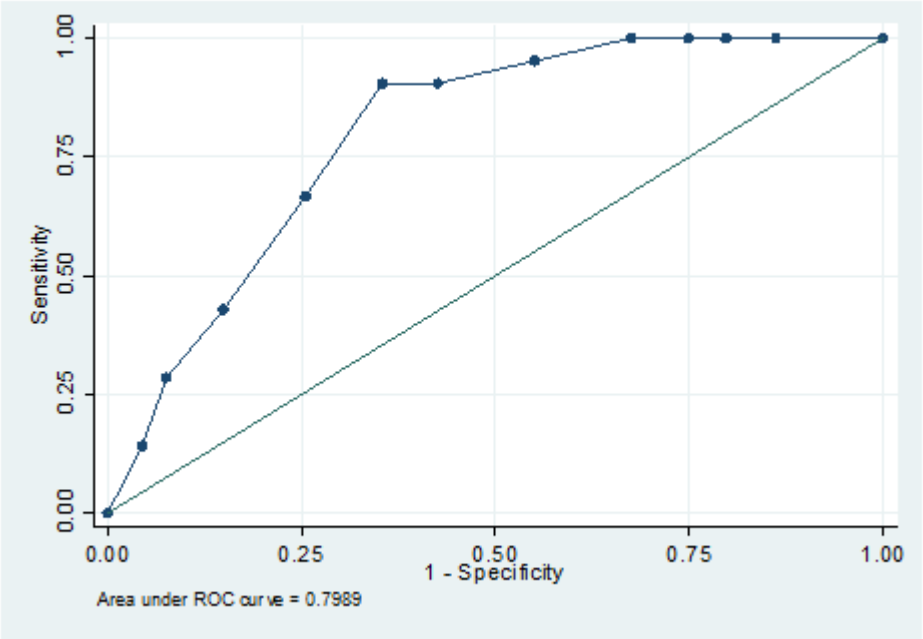

Figure 7-3 Performance of the New Score in KZN Data, Diagnosis by Fasting Glucose

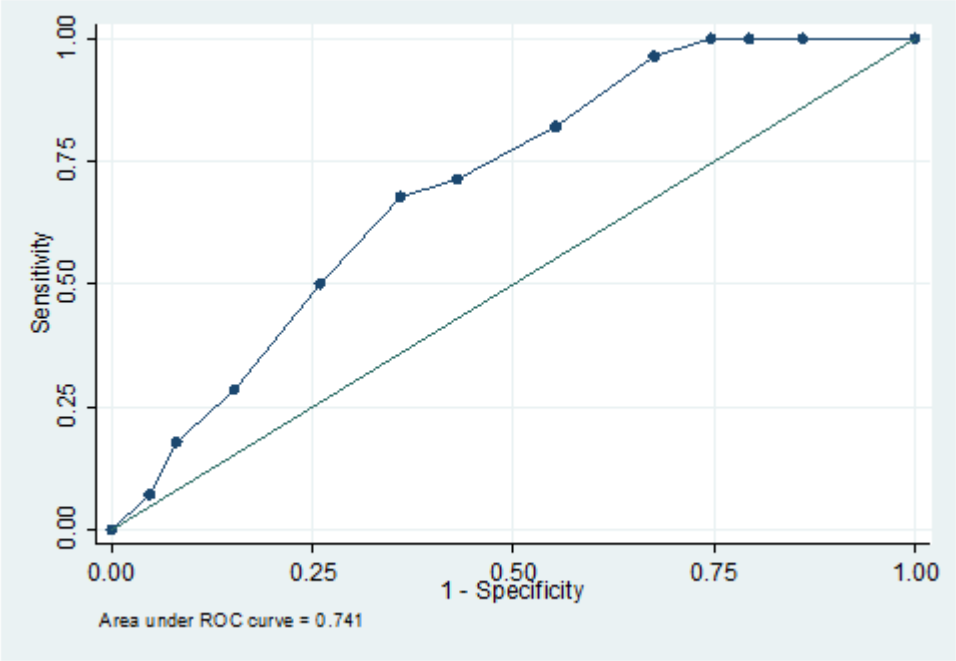

Figure 7-4 Performance of the New Score in KZN Data, Diagnosis by OGTT

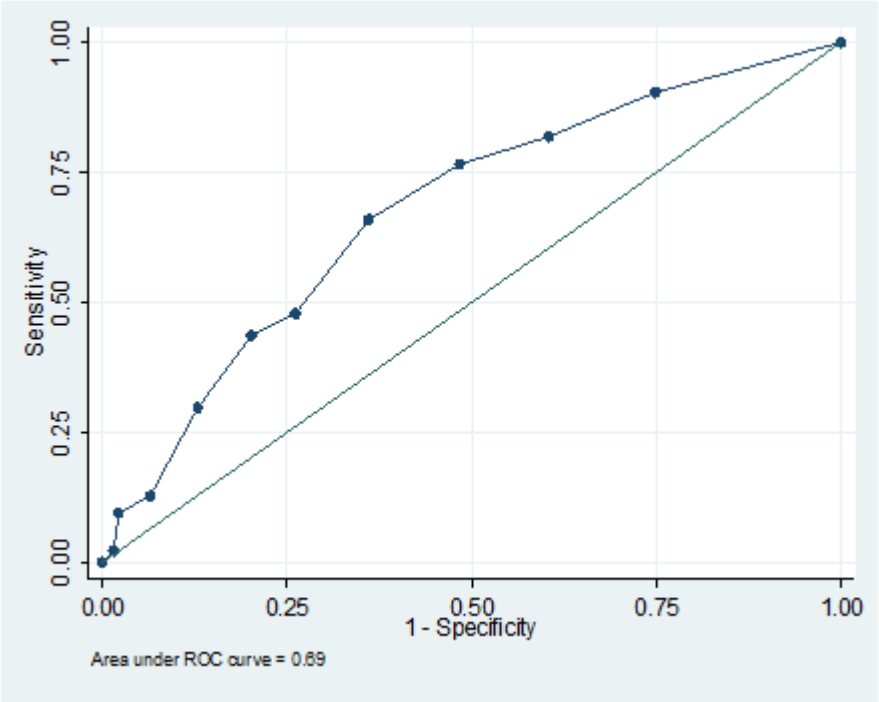

Figure 7-5 Performance of the New Score in Overall Guinea Validation Population

7.3.3 Comparison of the Performance of the New Model with Existing Risk Scores

The new score performed better when compared to the existing diabetes scores in the CRIBSA study population (Table 7-2).

In the CRIBSA study validation , compared to the KZN validation the US score (Bang et al., 2009) had similar performance when fasting glucose is used for diagnosis in both the Area under the ROC curve 0.79 (95% CI 0.73 to 0.85) vs. 0.76 (95% CI 0.69 to 0.84) and a better combination of sensitivity (66.7%) and specificity (77%) vs. sensitivity (50%) and specificity (82.4%) . The Rotterdam (Baan et al., 1999), Chinese (Gao et al., 2010) and the US score (Bang et al., 2009) displayed overall good combination of both sensitivity and specificity . The Indian scores (Chaturvedi et al., 2008, Ramachandran et al., 2005) had sensitivity of over 90% but had the lowest specificity of around 30%. When OGTT is used to define cases a similar pattern is observed in both AUC and in sensitivity and specificity with the US score (Bang et al., 2009) showing almost similar performance when compared to the new score developed in this study.

Table 7-2 Comparison of the Performance of the New Model with Existing Scores in CRIBSA Study Population

Score	AUC				Sensitivity (%)	Specificity (%)
		Std. Error	Lower Bound	Upper Bound		
FPG						
New score	0.82	0.029	0.76	0.87	80.0	72.4
Chinese score (Gao et al., 2010)	0.75	0.035	0.69	0.82	83.3	60.0
Oman score (Al-Lawati and Tuomilehto, 2007)	0.74	0.037	0.67	0.81	76.9	54.0
Brazilian score (Pires de Sousa et al., 2009)	0.72	0.038	0.65	0.79	80.0	45.9
Indian score (Ramachandran et al., 2005)	0.77	0.032	0.71	0.83	94.9	29.1
Indian score (Chaturvedi et al., 2008)	0.76	0.032	0.69	0.83	97.4	31.0
US score (Bang et al., 2009)	0.79	0.030	0.73	0.85	66.7	77.0
Rotterdam score (Baan et al., 1999)	0.73	0.039	0.65	0.81	62.5	70.3
2hr OGTT						
New score	0.75	0.041	0.56	0.82	68.9	71.2
Chinese score (Baan et al., 1999)	0.69	0.044	0.60	0.77	73.7	57.4
Oman score (Al-Lawati and Tuomilehto, 2007)	0.70	0.040	0.62	0.77	72.7	53.9
Brazil score (Pires de Sousa et al., 2009)	0.72	0.040	0.64	0.80	78.4	45.7
Indian score (Ramachandran et al., 2005)	0.70	0.039	0.63	0.78	91.0	43.4
Indian score (Chaturvedi et al., 2008)	0.69	0.041	0.61	0.77	84.4	29.4
US score (Bang et al., 2009)	0.75	0.037	0.68	0.82	60.0	77.2
Rotterdam score (Baan et al., 1999)	0.70	0.042	0.62	0.78	64.4	70.3

Key
FPG = Fasting Plasma Glucose, OGTT = Oral Glucose Tolerance Test, AUC = Area under the Curve, Std. Error = Standard Error of the AUC
The cut off used for the scores were ≥ 7 for the new score, ≥ 14 for the Chinese score (Gao et al., 2010), ≥ 10 for the Oman score (Al-Lawati and Tuomilehto, 2007), ≥ 18 for the Brazil score (Pires de Sousa et al., 2009), ≥ 21 (Ramachandran et al., 2005) and ≥ 16 (Chaturvedi et al., 2008) for the Indian scores, ≥ 5 for the US score (Bang et al., 2009) and ≥ 6 for the Rotterdam score (Baan et al., 1999).

Table 7-3 Comparison of the Performance of the New Model with Existing Scores in KZN Study Population

Score	AUC				Sensitivity (%)	Specificity (%)
		Std. Error	Lower Bound	Upper Bound		
FPG						
New score	0.80	0.035	0.77	0.83	90.5	65.0
Chinese score (Gao et al., 2010)	0.73	0.039	0.65	0.80	75.0	66.0
Oman score (Al-Lawati and Tuomilehto, 2007)	0.69	0.043	0.61	0.77	82.6	55.0
Brazilian score (Pires de Sousa et al., 2009)	0.64	0.042	0.56	0.72	54.5	57.6
Indian score (Ramachandran et al., 2005)	0.76	0.036	0.69	0.83	95.7	43.2
India score (Chaturvedi et al., 2008)	0.76	0.039	0.69	0.84	95.8	39.8
US score (Bang et al., 2009)	0.76	0.037	0.69	0.84	50	82.4
Rotterdam score (Baan et al., 1999)	0.61	0.052	0.51	0.71	48	68.8
2hr OGTT						
New score	0.70	0.040	0.62	0.78	67.9	64.0
Chinese Score (Gao et al., 2010)	0.67	0.039	0.59	0.74	68.8	66.0
Oman score (Al-Lawati and Tuomilehto, 2007)	0.65	0.040	0.58	0.73	71.9	54.8
Brazil score (Pires de Sousa et al., 2009)	0.58	0.044	0.50	0.67	48.3	47.4
Indian score (Ramachandran et al., 2005)	0.68	0.040	0.60	0.76	78.1	42.6
Indian score (Chaturvedi et al., 2008)	0.67	0.042	0.59	0.76	87.5	39.8
US score (Bang et al., 2009)	0.70	0.036	0.64	0.77	37.5	82.3
Rotterdam score (Baan et al., 1999)	0.58	0.048	0.48	0.67	39.4	68.7

Key
FPG = Fasting Plasma Glucose, OGTT = Oral Glucose Tolerance Test, AUC = Area under the Curve, Std. Error = Standard Error of the AUC
The cut off used for the scores were ≥ 7 for the new score, ≥ 14 for the Chinese score (Gao et al., 2010), ≥ 10 for the Oman score (Al-Lawati and Tuomilehto, 2007), ≥ 18 for the Brazil score (Pires de Sousa et al., 2009), ≥ 21 (Ramachandran et al., 2005) and ≥ 16 (Chaturvedi et al., 2008) for the Indian scores, ≥ 5 for the US score (Bang et al., 2009) and ≥ 6 for the Rotterdam score (Baan et al., 1999).

As mentioned previously in this chapter, in the Guinea validation study only the Brazilian (Pires de Sousa et al., 2009) score could be validated due to lack of appropriate variables in the data sets, the results of which are stratified by sex categories because of enough events per variable. In this population the performance of the new risk score (AUC 0.69 95% CI 0.64 to 0.75) was lower compared to when it was applied to the KZN (AUC 0.80 95% CI 0.77 to 0.83) and CRIBSA study populations (AUC 0.82 95% CI 0.76 to 0.87). The score however had a non-significant better performance among females compared to males, AUC 0.7 (95% CI 0.63 to 0.77) vs. 0.65 (95% CI 0.57 to 0.73) respectively. The new score had much lower sensitivity among males (33%) compared to females (53%). The Brazilian score had poor performance in this population with especially low sensitivity ranging from 29% to 35% respectively but with good specificity of more than 70%.

Table 7-4 Performance of the New Risk Score in Comparison with Existing Scores in the Guinea Validation Population

Score	AUC				Sensitivity (%)	Specificity (%)
		Std. Error	Lower Bound	Upper Bound		
FPG						
New score Overall	0.69	0.027	0.64	0.75	43.6	79.8
New score Male	0.65	0.042	0.57	0.73	33.3	83.7
New score Female	0.70	0.037	0.63	0.77	53.1	76.4
Brazil score (Pires de Sousa et al., 2009) Overall	0.62	0.027	0.57	0.67	31.9	77.8
Brazil score (Pires de Sousa et al., 2009) Male	0.58	0.041	0.50	0.66	28.8	78.2
Brazil score (Pires de Sousa et al., 2009) Female	0.66	0.035	0.59	0.73	34.7	77.4

Key
FPG = Fasting Plasma Glucose, AUC = Area under the Curve, Std. Error = Standard Error of the AUC
The cut off used for the scores were ≥ 7 for the new score and ≥ 18 for the Brazil score (Pires de Sousa et al., 2009)

7.4 Discussion

This chapter was aimed at externally validating the derived new diabetes score in new populations and to compare its performance with existing scores. The existence of effective means for the prevention and control of diabetes have spurred the importance of diabetes risk scores as a public health tool to identify individuals at high risk of diabetes. In this study 7 existing risk scores are evaluated alongside the new score in various populations. All the existing risk scores were evaluated using the optimal cut off points as described in the original studies shown in Table 7-1.

The performance of the newly derived risk score in the validation samples was comparable to the performance in derivation study population with Area under the ROC curve ranging from 0.70 to 0.82 despite using the point score rather than the regression equation which tends to lower performance if the former is used. This performance is good compared to score performance at validation (AUCs) reported in previously published scores where in some validation studies the score performance had wide uncertainty intervals. For example, the Rotterdam score (original performance AUC 0.68, 95% CI 0.64 to 0.72) (Baan et al., 1999) performance ranged from AUC of 0.53 (95% CI 0.48 to 0.71) in the Cameroonian and in the Oman populations (95% CI 0.53 to 0.54) to 0.70 (95% CI 0.67 to 0.73) when validated in the Australian, US 0.68 (95% CI 0.64 to 0.71) and in the Danish 0.69 (95% CI 0.65 to 0.72) populations (Glumer et al., 2006).

Another score that has reportedly been externally validated is the Indian diabetes score (original performance AUC 0.73 95% CI 0.70 to 0.76) (Ramachandran et al., 2005) with performances ranging from AUC of 0.63 (95% CI 0.60 to 0.65) in the Chinese population (Gao et al., 2010) to AUC of 0.70 (95% CI 0.66 to 0.74) in the Taiwanese population (Lin et al., 2009). The Danish score (original performance AUC 0.80 95% CI 0.76 to 0.83) shows significantly less performance at external validation in the Chinese population AUC 0.70 (95% CI 0.66 to 0.71) but comparable performance 0.75 (95% CI 0.71 to 0.78) in the Australian population.

Of the scores validated in this study 3 scores have also been externally validated. These include the Rotterdam (Baan et al., 1999), the Indian (Ramachandran et al., 2005) and the Oman (Al-Lawati and Tuomilehto, 2007) score. Compared to performance in the validation populations in this study, the Rotterdam score, for example, had an AUC of

0.68 (95% CI 0.64 to 0.72) in the original population with sensitivity and specificity of 55% and 78% respectively, and at validation the score had a non-significant better performance in the CRIBSA study population with an AUC of 0.73 (95% CI 0.65 to 0.81) and sensitivity of 63% and specificity of 70%. Whilst in the KZN study population the performance was non-significantly lower with AUC of 0.61 (95% CI 0.51 to 0.71) and sensitivity and specificity of 48% and 69% respectively.

The Oman risk score in this population in this validation study had an AUC of 0.74 (95% CI 0.67 to 0.81) and sensitivity and sensitivity of 77% and 54% in the CRIBSA study population and AUC of 0.70 (95% CI 0.61 to 0.77) and sensitivity and specificity of 83% and 55% respectively which is lower compared to the score performance in the original population (AUC 0.83 95% CI 0.82 to 0.84, sensitivity 79% and specificity 73%). The performance of the score has shown consistent results when this validation performance is compared to what was reported when the Oman score was validated in the Taiwanese population where the AUC was reported to be 0.72 (95% CI 0.69 to 0.75) (Lin et al., 2009).

The Indian risk score developed by Ramachandran et al had good performance when applied to both the CRIBSA (AUC 0.77 95% CI 0.71 to 0.83) and the KZN (AUC 0.76 95% CI 0.69 to 0.83) study populations which is non-significantly higher compared with the performance in the original population (AUC 0.73 95% CI 0.70 to 0.76) in terms of the ability to discriminate cases from non-cases measured as the Area under the ROC curve, but the score had varying performance in terms of sensitivity and specificity both in this study and other studies that had previously validated the score. In the original population this score had sensitivity and specificity of 77% and 60% respectively. At validation in the CRIBSA study population this score had sensitivity and specificity of 97% and 29% respectively and in the KZN population the score had sensitivity and specificity of 96% and 43% respectively. These results are similar to what was reported by Gao (Gao et al., 2010). When the score was applied to the Chinese population in this study the score had sensitivity of 96% but poor specificity of around 19%.

Many risk scores show worse performance when applied to populations other than the original population where the score was developed. However, in this study we have shown contrary findings in that some of the scores, for example the Rotterdam and the Indian risk scores, had better discrimination statistics at validation although the differences did not reach statistical significance. This could be explained by the high

prevalence of the outcome in the validation population. For example, the CRIBSA study population (see chapter 6 on page 76) had a high diabetes prevalence of 12%, had higher mean BMI (29% kg/m^2) and had higher prior history of diabetes (30%). To support this hypothesis the Rotterdam score had a lower performance in the KZN study population which had much lower diabetes prevalence (4.3%), lower mean BMI (25.5 kg/m^2) and a lower prevalence of hypertension history (16%) compared to the original population.

One reason for the consistent performance for example of the Oman risk score is the use of predictor variables that can be measured consistently across populations; this model incorporates only age, waist circumference, BMI, family history of diabetes and current hypertension status. Behavioral variables such as diet and physical activity measures may be difficult to be ascertained because they may be affected by cultural diversity and therefore affect the accuracy of the measurements. This is reflected by the poor sensitivity and specificity at validation and requires adjustment of the cut-off point to improve performance as illustrated previously by Al Lawati and Colleagues when they validated different scores using both the optimal cut off in the original study and the adjusted cut off to fit the Kuwaitian population (Al-Lawati and Tuomilehto, 2007). Also because many scores incorporate anthropometry measures, whose cut offs are dependent on ethnicity risk scores derived in Whites and Asian, for example, they will have poor performance in estimating risk resulting in poor sensitivity and specificity e.g. the Indian and the Chinese risk scores (Chaturvedi et al., 2008, Mohan et al., 2005, Ramachandran et al., 2005, Gao et al., 2010).

The relationship between sex and diabetes varies across settings with the risk in males being clearer in White populations and this could explain the poor performance of the risk scores (Bang et al., 2009, Baan et al., 1999) that incorporate sex as a predictor variable, especially in African settings where this relationship is unclear.

The study is not without limitations, firstly not all the scores could be validated because of the lack of some of the predictor variables in the scores, and also the validation data sets had more women than men which could further affect the overall performance of the scores. Missing data in some of the data sets is another challenge which could potentially introduce bias. It should also be noted that the validation data sets used different methods for diabetes diagnosis which could have potentially affected the performance of the scores.

The validation of the different scores was done using the simplified point based risk scores presented by authors in the various studies instead of applying the original model; which normally lowers the model performance. But it should be noted that the results on performance of the original scores presented by the study authors were all calculated using the point scores. An attempt was made to contact the authors to make comparison between the performance of point based score and the original score, but information could not be obtained as most authors did not report the y – intercept from for their full models.

It should be noted that the performance of the scores (sensitivity and specificity) is dependent upon the level of cut-off point as highlighted previously and also the prevalence of disease in a particular population, this could have affected the performance of the scores in the validation studies. The higher the prevalence of diabetes, the higher the probability of a positive test and the reverse is also true. The scores would probably have a different performance had the appropriate cut off point been applied, no attempt was made to modify the score to enhance the performance because it was beyond the scope of this study. The main advantage of this study is that it had adequate sample size for validation for the number of variables in the validated scores.

The results of the present study are significant in respect to the future direction of diabetes screening. Combining more than one population in deriving the risk score could potentially lead to a risk score that can be broadly applied across different populations and also by using variables that are not ethnic or culturally specific the performance of the scores can be enhanced, this could potentially explain the good performance of the US score which was developed using multi-ethnic population (Bang et al., 2009). Secondly, this study affirms the previous recommendation that before the score is adapted for use in a given population it should be validated and adjusted accordingly to suit that particular population. Methods of updating the risk scores to a new population have been described (Steyerberg, 2009) and more efforts should be directed towards evaluating the existing scores and adapting them to local settings.

More research is needed however in this area to validate the utility of such a score in different settings, and so more research is needed to elucidate the impact and cost effectiveness of using these risk scores as a public health tool towards prevention of diabetes and its complications.

There is also the need to study how the score would work in clinical practice before rolling out a screening program. An evaluation of the UK pilot diabetes screening revealed that there were a lot of unanticipated challenges from implementing the screening program in a non-trial setting. The findings showed inconsistency in implementing the screening protocol, lack of quality control, lack of adequate diagnostic testing and follow up after a positive test (Goyder, 2008) which affected the overall effectiveness of the intervention.

Another interesting area of research is to look at the performance of scores derived to predict undiagnosed diabetes for prediction of future development of diabetes in disease free individuals.

Chapter 8. Validation of the Model in a Clinical Setting and Comparison of the New Model Performance to Existing Models

8.1 Introduction

Chapter 7 described the performance of the new risk score across different validation populations using data from studies in South Africa and Guinea different from the score derivation population. As previously established the performance of a score tends to be better in populations in which they were derived and it is important to validate the performance across new settings. The aim of this chapter is to evaluate the performance of the newly developed score across a different context from the score derivation population. The data for deriving the score were obtained from diabetes population based surveys where subjects were chosen at random during community surveys, the sampling process of these studies is described in details in Chapter 5 above. This chapter explores the performance of the score in a pragmatic setting where there is no random selection of participants; enrolment was rather based an open invitation on fulfilling a certain selection criteria. The criterion for selection was that the participants had to be above the age of 34 years and living in Dar es Salaam. The decision to include only those above the age of 34 was to increase the proportion of individuals with diabetes given that the prevalence of diabetes is low in younger age groups as outlined in Chapter 2 pg. 13.

This setting represents rather a different contextual setting form the score development. Apart from looking at the overall performance of the new score in comparison to other existing scores, this chapter looks at details the outcome of applying the score in terms of the characteristics of the populations by the outcomes of applying the new score to the populations.

To explore the usefulness of applying the score to screen for undiagnosed diabetes in this setting, a detailed account of characteristics and a comparison of the study populations is made between different categories of risk score points and across different diagnostic categories; true positives, false positive, true negative and false negatives obtained by applying the new score at a pre specified cut off point. Also this chapter looks at the yield of applying the score at different cut points in terms of the numbers needed to screen to identify one case of diabetes and the subsequent number of people that have been

identified correctly into the respective categories whether positive or negative for the condition being screened.

8.2 Methods

8.2.1 Study Population

Data used for validating the score is from screening individuals at district hospitals in Dar es Salaam Tanzania. People were invited to participate for diabetes screening to their local district hospitals in Dar es Salaam. Detailed accounts of the data collection methods and participants' characteristics are provided in chapter five on Overview of Study Populations page 76. This population represents a different setting compared to the score derivation population and the South African and Guinea validation populations. In the clinical validation population individuals were not selected at random therefore likely to contain a more homogenous population with individuals who are more likely to be older and or at high risk, which could be a source of bias but represent a pragmatic setting if the derived score were to applied as a screening tool at a hospital setting.

8.2.2 Assessment of Performance

The ability of the new score to discriminate between those with and without diabetes was assessed using Area under the Receiver Characteristic Curves (AUCs) and calibration compared using box plots and calibration slopes (Steyerberg, 2009) . Calibration slopes were calculated as the differences in the mean predictions in those with and without the disease (Steyerberg, 2009).

Clinical utility (diagnostic capacity) of the score was assessed using sensitivity, specificity and positive and negative predictive values (Herman et al., 1998). In addition participants' characteristics across diagnostic groups (true positives, true negatives, false positives and false negatives) were compared using Kruskal-Wallis test (Hennekens and Buring, 1989) . To calculate sensitivity and specificity of the score for comparison with existing ones, the cut-off point for the new score was set at a score of ≥ 7. The yield of the new score was further assessed at various cut points by the numbers needed to screen to identify one case of diabetes and the percentage of subjects with diabetes that were identified. The number needed to screen was calculated as the ratio of total number of undiagnosed diabetes cases diagnosed and the total number needed to be screened with the confirmatory test.

8.2.3 Risk Scores for Validation

In addition to the new model, all risk scores applied in chapter 8 on page 128, were also validated in this population to compare the performance of existing models and of the new model to this populations.

8.3 Results

8.3.1 Score Performance

The performance of the new score when applied to the Tanzania validation data is shown in Figure 8-1, Figure 8-2 and Table 8-1 below. The new score had an overall performance (AUC) of around 0.67 (95% CI 0.63 to 0.70) (Figure 8-1) with higher performance in males (AUC 0.69 95% CI 0.62 to 7.60) than in females (AUC 0.64 95% CI 0.62 to 0.74) see Figure 8-2. This performance is slightly lower than what was found when the score was validated in the CRIBSA and KZN and Guinea data with AUC ranging from 0.70 (95% CI 0.70 to 0.75) (Figure 7-5) in the Guinea validation population with lowest performance to 0.82 (95% CI 0.76 to 0.87) in the Cape Town study population (Figure 7-1). Table 8-1 below shows the performance of the new risk score in comparison with existing scores (Pires de Sousa et al., 2009, Al-Lawati and Tuomilehto, 2007, Baan et al., 1999, Bang et al., 2009, Chaturvedi et al., 2008, Gao et al., 2010, Ramachandran et al., 2005) in this population. The overall performance of existing scores ranged from an AUC of 0.58 (95% CI 0.54 to 0.61) for the Brazilian (Pires de Sousa et al., 2009) and Oman AUC 0.58 (95% CI 0.54 to 0.61) (Al-Lawati and Tuomilehto, 2007) scores, and the highest performance was shown with the US (Bang et al., 2009) score which had an AUC of 0.64 (95 CI 0.60 to 0.67) . The Chinese score (Gao et al., 2010) and a relatively better combination of sensitivity (76%) and specificity (45%) compared to the other existing scores. The Indian scores (Chaturvedi et al., 2008, Ramachandran et al., 2006) had high sensitivities ranging from 83% to 89% but very poor sensitivity ranging from 20% to 27% at the defined cut off points. The new score had moderately good sensitivity and specificity with sensitivity of 74% and specificity of 57%. Figure 8-2 shows the performance of the new score was better in males compared to females. In males the sensitivity and specificity of the new score was 70% and 65% respectively whilst in females it was 67% and 60% respectively. A similar pattern also emerged with all the existing scores when the analysis was done by sex, with all the scores having better performances in males compared to females in this population. The reason for the better

performance in men could be due to better correlation of the anthropometric measures (BMI and waist circumference) with diabetes risk in men compared to women.

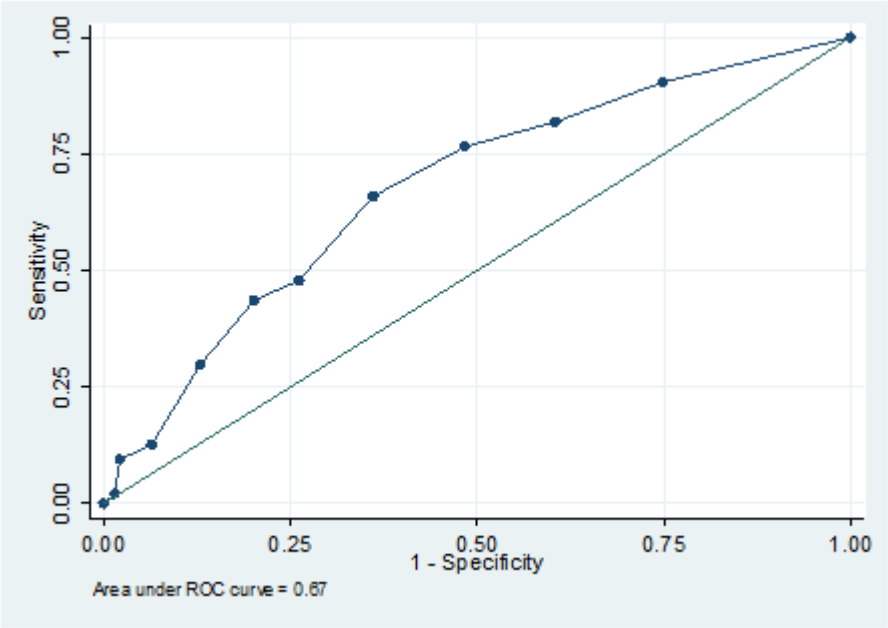

Figure 8-1 Performance of the New Score in the Tanzania Validation Population

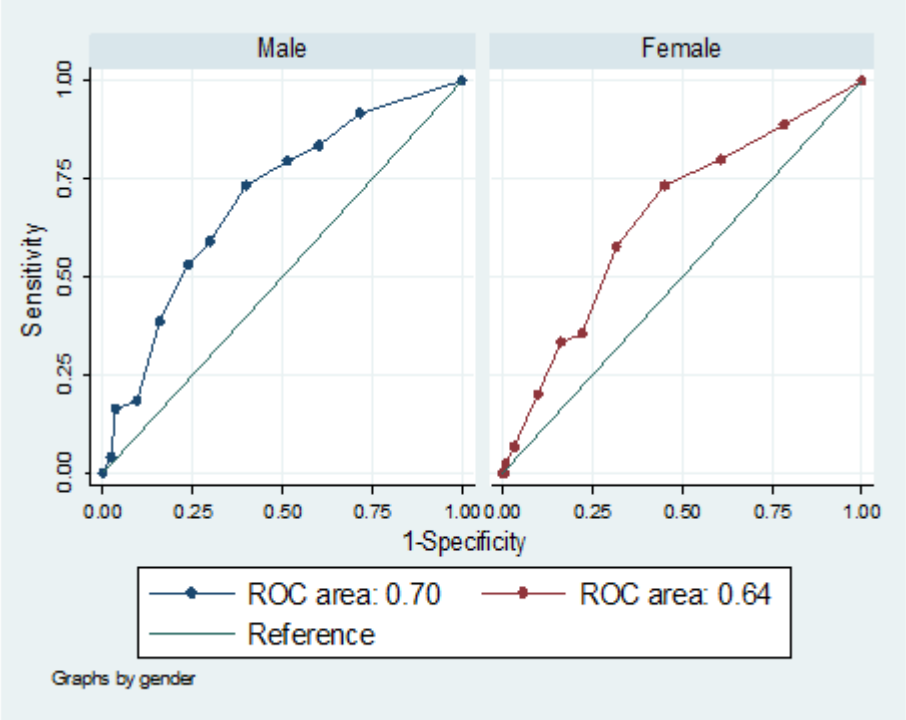

Figure 8-2 Performance of the New Score by Sex in the Tanzania Validation Population

Key
ROC = Receiver Operating Characteristic Curve

The calibration of the risk scores was assessed using calibration slopes, the higher the slope the better the distinction between those with and without the disease, with majority of cases without diabetes having scores below the cut-off point and those with diabetes having total scores above the cut- off point. In the derivation population the calibration was better in males with a calibration slope of 5 vs. a slope of 3 in females Figure 8-3, the findings also shows that the new score overestimated risk especially in women. In the validation population the calibration slopes were 5 for males and 4 for women slightly better than what was observed in the derivation population.

Table 8-1 Performance of the New Score Compared to Existing Scores in the Tanzania Validation Study

Score	AUC				Sensitivity %	Specificity %
		Std. Err.	Lower Bound	Upper Bound		
OVERALL						
New score	0.67	0.03	0.63	0.70	74.3	57.1
Chinese score (Gao et al., 2010)	0.63	0.03	0.59	0.66	75.9	45.4
Oman score (Al-Lawati and Tuomilehto, 2007)	0.58	0.03	0.54	0.61	65.4	40.6
Brazil score (Pires de Sousa et al., 2009)	0.58	0.03	0.54	0.61	60.4	48.4
India Score (Ramachandran et al., 2005)	0.61	0.03	0.58	0.64	83.5	27.2
India Score (Chaturvedi et al., 2008)	0.62	0.03	0.58	0.64	89.2	20.1
Us Score (Bang et al., 2009)	0.64	0.03	0.60	0.67	32.0	84.4
Rotterdam (Baan et al., 1999)	0.60	0.03	0.57	0.63	44.9	69.6
MALE						
New score	0.69	0.03	0.62	7.60	70.0	65.0
Chinese score (Gao et al., 2010)	0.66	0.04	0.58	0.73	89.6	39.8
Oman score (Al-Lawati and Tuomilehto, 2007)	0.59	0.04	0.50	0.67	60.0	52.5
Brazil score (Pires de Sousa et al., 2009)	0.62	0.04	0.53	0.71	54.5	58.1
India Score (Ramachandran et al., 2005)	0.65	0.04	0.58	0.73	87.2	39.5
India Score (Chaturvedi et al., 2008)	0.66	0.03	0.58	0.74	91.3	31.2
Us Score (Bang et al., 2009)	0.66	0.04	0.57	0.74	38.3	80.8
Rotterdam (Baan et al., 1999)	0.61	0.04	0.52	0.70	63.3	52.6
FEMALE						
New score	0.64	0.03	0.54	0.74	67.0	60.2
Chinese score (Gao et al., 2010)	0.58	0.04	0.50	0.66	64.3	47.7
Oman score (Al-Lawati and Tuomilehto, 2007)	0.58	0.04	0.50	0.66	69.6	35.7
Brazil score (Pires de Sousa et al., 2009)	0.58	0.04	0.50	0.66	66.0	44.3
India Score (Ramachandran et al., 2005)	0.60	0.04	0.51	0.68	80.4	22.0
India Score (Chaturvedi et al., 2008)	0.60	0.04	0.51	0.67	83.9	28.6
Us Score (Bang et al., 2009)	0.61	0.04	0.52	0.69	26.8	85.9
Rotterdam score (Baan et al., 1999)	0.54	0.04	0.47	0.62	29.3	76.6

Key
FPG = Fasting Plasma Glucose, OGTT = Oral Glucose Tolerance Test, AUC = Area under the Curve, Std. Error = Standard Error of the AUC
The cut off used for the scores were ≥ 7 for the new score, ≥ 14 for the Chinese score (Gao et al., 2010), ≥ 10 for the Oman score (Al-Lawati and Tuomilehto, 2007), ≥ 18 for the Brazil score (Pires de Sousa et al., 2009), ≥ 21 (Ramachandran et al., 2005) and ≥ 16 (Chaturvedi et al., 2008) for the Indian scores, ≥ 5 for the US score (Bang et al., 2009) and ≥ 6 for the Rotterdam score (Baan et al., 1999).

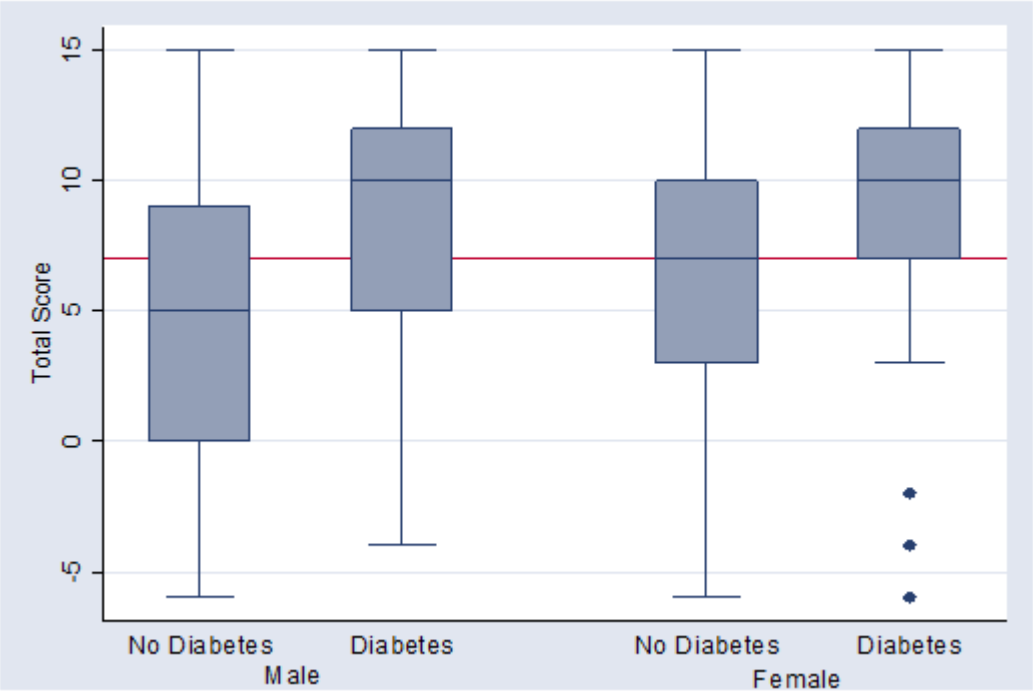

Figure 8-3 Calibration of the New Score in the Derivation Population

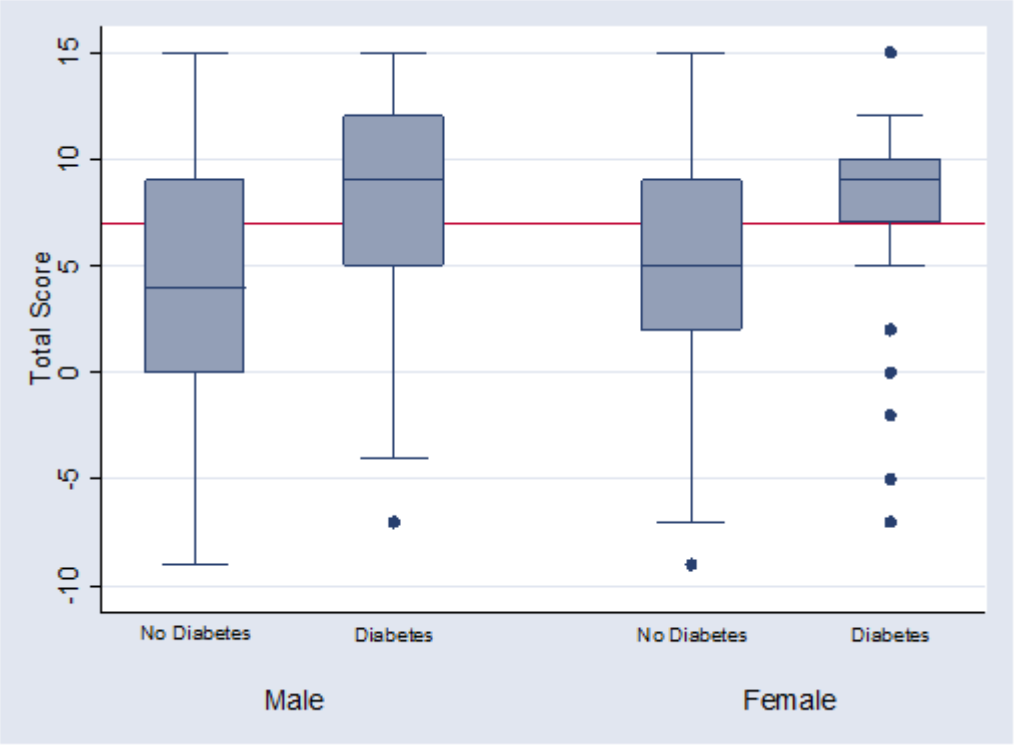

Figure 8-4 Calibration of the New Score in the Clinic Validation Population by Sex

Key
Box plots showing score calibration in derivation and validation in the clinic study population, the higher the mean score above the red reference line for those with diabetes the better the discrimination, and the lower the mean score below the reference line for those without diabetes the better the calibration, these graphs are showing that in both cases calibration was better in males.

8.3.2 Yield and Characteristic of Study Participant across Diagnostic Categories

The yield (number of people diagnosed) of the score or clinical utility of the score is summarized in Table 8-2 and

Table 8-3 below. Table 8-2 shows the yield of the score across different diagnostic categories and summarizes the number that will need to be screened with a subsequent test and the numbers needed to screen to identify one case of diabetes and also the percentage of those with undiagnosed diabetes that are diagnosed when the risk score is used for diagnosis.

At the recommended cut off point of ≥7 the score has sensitivity and specificity of 74% and 57% as mentioned previously and a positive predictive value of 16.4 (Table 8-2). Using this cut off point (≥7) 46% of the participants will require a confirmatory test and the number needed to screen to identify one diabetes case is reduced to 8 from 20 in this population at the cost of missing one case out of every five.

Results also show that increasing the cut off points increases the specificity at the expense of sensitivity and reduces significantly the number of cases of undiagnosed diabetes that would be picked, for example increasing the cut-off point from ≥7 to ≥ 9 reduces the percentage of diabetes cases identified from 74% to 59%. Figure 8-5 also shows that the proportion of participants with diabetes increased sharply from around 5% among those with total scores of 5 or less than 5 to more than 15% in those with total scores of more than 5.

Table 8-3 summarizes the characteristics of patients across different diagnostic categories namely true positives, true negatives, false positives and false negatives. Results show that both the true positives and false positives are individuals at high risk with higher levels of cardiovascular risk profiles; are older, obese, have hypertension, and have high cholesterol levels compared to the true negatives and the false negatives. The individuals with undiagnosed diabetes that are missed by the score are younger, with lower mean blood pressure and are less obese.

Table 8-2 Yield of Using the Score to Screen for Undiagnosed Diabetes across Different Categories

Total score	Sensitivity (95% CI)	Specificity (95% CI)	LR+	PPV	N (%) Screen	Prevalence	% Diagnosed	NNs
≥0	91.4 (84.4 to 96.0)	16.5 (14.2 to 19.1)	1.1	11.0	870 (84.0)	5.0%	91.0	20
≥3	82.9 (74.3 to 89.5)	34.8 (31.8 to 38.0)	1.27	12.6	691(66.9)	4.3%	82.9	23
≥5	78.1 (69.0 to 85.6)	46.1 (42.8 to 49.3)	1.45	14.1	582(56.4)	3.8%	78.1	21
≥7	74.3(64.8 to 82.3)	57.1 (53.8 to 60.3)	1.73	16.4	476 (46.1)	12.4%	74.3	8
≥9	59.0 (49.0 to 68.5)	69.3 (66.2 to 72.2)	1.92	17.9	347(33.7)	19.3%	59.0	5
≥12	29.5 (21.0 to 39.2)	83.2 (80.6 to 85.5)	1.75	16.6	187(18.0)	16.6%	29.5	6

Key
NNS= Number Needed to Screen
CI = Confidence Interval
LR+ = Likelihood ratio of a positive test
PPV = Positive Predictive Value
N= Number of people requiring a confirmatory test

Table 8-3 Characteristics of Study Participants across Different Diagnostic Categories

	Diagnosis Category					
Variables	**TP**	**FP**	**FN**	**TN**	**All**	**P value**
Age (yrs.)	55.2 (10.3)	54.3(10.2)	44.3(8.9)	40.63 (10.7)	47.1(12.5)	<0.001
BMI (kg/m2)	29.3 (4.7)	30.15 (6.0)	22.93(5.1)	24.95(5.1)	27.2(6.0)	<0.001
Waist Circumference (cm)	103.8 (18.5)	101.8(10.6)	82.11(12.8)	85.8 (11.3)	93.2 (14.4)	<0.001
Systolic BP	147.3 (23.4)	149.4(26.0)	123.6(17.3)	122.0(18.0)	134.5 (25.6)	<0.001
Diastolic BP	87.0(13.9)	88.2 (13.2)	77.7 (11.9)	74.8(12.0)	81.0 (14.2)	<0.001
Total Cholesterol	6.1(2.0)	6.2(2.1)	5.6(1.5)	5.5(1.8)	5.8(1.9)	<0.001
HDL Cholesterol	1.4(0.7)	1.5(0.5)	1.5(0.6)	1.5(0.5)	1.5(0.5)	0.205
Triglycerides	1.3(0.9)	1.2(0.9)	1.2(0.9)	0.9(0.7)	1.1(0.8)	<0.001

Key
Values are means (standard deviation), P Value for differences between groups
TP= True Positives, FP= False Positives, FN = False Negatives, True Negatives

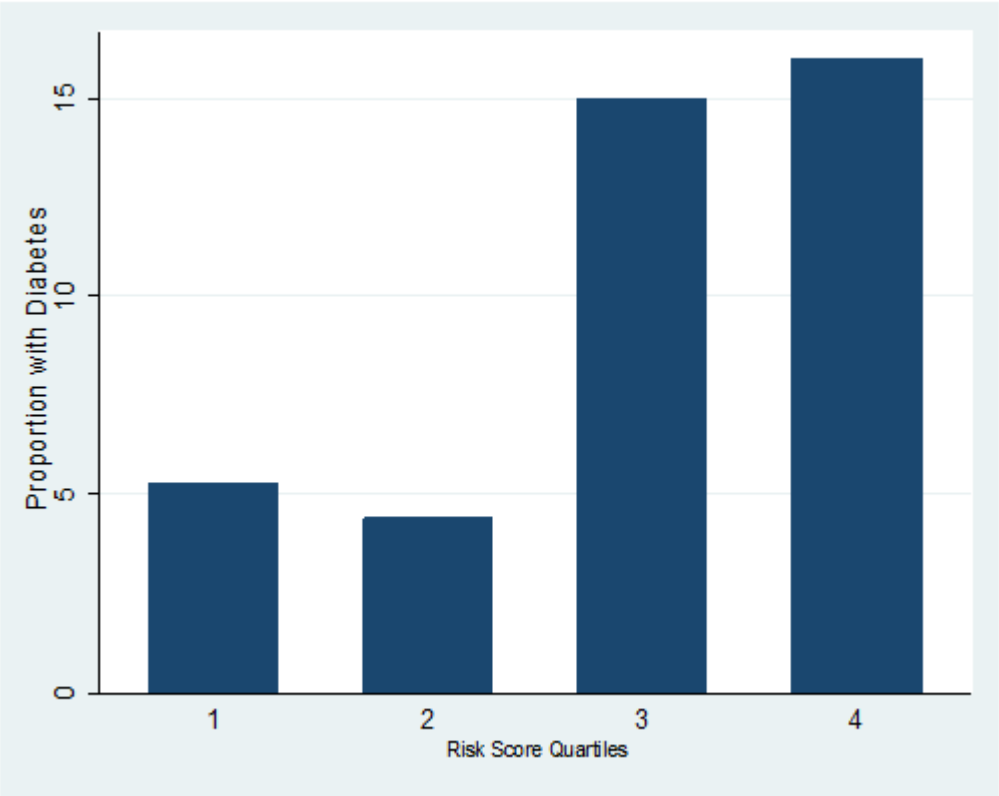

Figure 8-5 Proportion with Diabetes across Risk Score Quartiles

Key
1= Total score of -9 to 2,
2= Total score of 3 to 5,
3= Total score of 6 to 10
4= Total score 11 to 15

8.4 Discussion

This chapter dealt with the validation of the newly derived score in a pragmatic clinical (where the score would be applied for screening at a hospital) setting. The chapter specifically sought to determine the yield and the effectiveness of applying the score to screen for undiagnosed diabetes.

The score performance in this population was lower than what was found in the previous chapters where the score was applied to populations of South African origin chapter 7. Ewout 2009 (Steyerberg, 2009) suggests that external validity of a risk prediction is affected by two main factors first is the validity of the regression coefficients which is affected by the differences in the relationship between the validation and the developmental study population, this could be due to true differences or differences in the definition of predictors and the outcome and differences in the selection of patients. Also the differences could arise from a narrow selection of cases which he termed homogeneous case mix. The later theory explains better the drop of performance in this study due to the non-random selection of study and the nature of how the patients were recruited the participants that were recruited were somewhat homogenous with high levels of risk factors hence affected the discriminatory capacity of the score without affecting its calibration. This findings show that the performance of the score would actually be better in populations with more heterogeneous case mix for example in settings where the participants are selected at random which was the case for the south Africa and the Guinea validation populations. The better performance of the score in men compared to women could be due to the fact that waist circumference has better correlation with diabetes risk in men.

In evaluating screening tests one of the important characteristic besides the discrimination and the calibration statistics is the yield of screening. The yield of screening is affected by the prevalence of the target disease in the background population. In settings where prevalence of the outcome is low screening everyone may not be worthwhile as the yield may be very low (Janssen et al., 2007, Leiter et al., 2001). The yield can be enhanced by targeting a group of individuals with high probability of the outcome. Risk scores and using other demographic characteristics can be used to identify individuals at high risk.

For example the Nationwide screening that was carried out in Brazil (Nucci et al., 2004, Toscano et al., 2008) identified one case of diabetes for every 64 people screened translating into a cost of 76 USD to identify one case of diabetes. The cost could have been significantly reduced if an initial screening test was used to identify high risk individuals. In settings where the prevalence of diabetes is high universal screening may be cost effective for example in Saudi Arabia one of the countries with highest prevalence of diabetes needed to screen 6 individuals to identify one case of diabetes in a community wide screening that was carried out (Al-Baghli et al., 2010). In this study applying the risk score reduced the number needed to screen from 20 to 8 which similar findings compared to what has been reported in other studies for example a study in Japan reported a reduction of the number needed to screen from about 16 to less than 7 when age, BMI, hypertension history was used to pre-screen individuals before going for a secondary test.

This study has shown that screen detected high risk individuals are at higher levels of cardiovascular risk factors regardless of their diabetes status. These findings agree with what has been reported previously in other studies. A study in the Netherlands (Janssen et al., 2008) demonstrated that high risk individuals free of diabetes identified at screening had high levels of cardiovascular events and should not be re-assured but intervened upon to reduce their risk of bad cardiovascular outcomes. Other studies also report similar findings, for example a study by Sandbaek et al (Sandbaek et al., 2008) showed that individuals with high risk score had significantly higher mortality compared to those within the lower risk score categories in the ADDITION study . In this study it was found that the individuals with diabetes who are missed by the score have lower cardiovascular risk profiles and a study previously demonstrated that this group of individuals was shown to have significantly lower risk of mortality compared to the true positives and the false positives (Spijkerman et al., 2002).

The cost screening for diabetes is dependant over several factors including, the type of test used and the cut off points used for diagnosis, the test uptake, frequency of testing, and most importantly what happens to those diagnosed with diabetes or having prediabetes. Studies have previously reported that screening is more cost effective if a diabetes risk score or a form of risk stratification such as age and obesity is applied to stratify individuals at high risk who are then invited (Zhang et al., 2003, Mohan et al., 2011). The type of glucose test used also affect the overall cost of screening, due to the

cost of individual test (HbA1c more costly compared to FBG or RBG) or the overall test uptake, with studies showing that OGTT screening strategies with OGTT were less cost effective if the OGTT uptake was low (Hoerger et al., 2004, Icks et al., 2004, Icks et al., 2005, Janssen et al., 2007). Most studies have shown that diabetes screening is more cost effective if started above the age of 40 years and if repeated after every 3 to 5 years, frequent screening or screening those below the age of 40 are less likely to be cost effective because it leads to low yield due to resulting low prevalence (Kahn et al., 2010, Gillies et al., 2008).

For a screening program for undiagnosed diabetes, the underlying assumption is that people with diabetes will be diagnosed early and referred for proper care. Studies looking at effectiveness of diabetes screening have shown that this is a key underlying factor that determines cost effectiveness (Gillies et al., 2008, Kahn et al., 2010, Li et al., 2010). Availability of organised care and follow up of cases identified through screening is likely to be a challenge if this risk score is to be applied in practice, as outlined in chapter three on page 32; diabetes screening in Sub-Saharan Africa will require further investment in strengthening the health care system.

In conclusion screening for diabetes may be worthwhile but likely to be challenging especially Sub Saharan Africa. Studies have demonstrated that individuals that are labelled high risk by the risk scores tend to have higher risk of cardiovascular diseases and mortality and that it is worthwhile to intervene in this group of individuals regardless of their diabetes status. Use of diabetes risk scores also significantly reduces the overall cost of screening and increases the yield of the screening program.

Chapter 9. Conclusion

This study has given an account of the burden of diabetes in Africa and the opportunities for earlier identification of people at high risk of diabetes and its complications. It is evident that the prevalence of diabetes and its related complications are increasing in Africa and globally as a whole. Strategies are needed to ensure that the current trends in the increase in the burden of diabetes do not continue.

This study was designed to develop and validate a diabetes screening tool for use in low resource settings in Africa, and also describes the performance of diabetes risk scores derived from other populations when applied to the African populations. The study pooled data from 3 African countries with the aim of developing a risk score that would be applicable across a wider African setting.

The resulting score has age, waist circumference and prevalent and or history of hypertension as predictor variables. In this study when the existing scores were validated, it is worth noting that the scores did not differ much in their ability to discriminate between cases and non-cases based on the AUCs, but calibration was poor for all the scores. The following conclusions can be drawn from the present study; the performance of the new score developed in this study was better across all populations where it was validated in terms of both discrimination and calibration. Also the score performance can be enhanced by re calibrating the score to the new populations where it is intended to be applied (Steyerberg, 2009). The present study confirms previous findings that risk scores may not apply universally as it has generally been demonstrated by previous studies, and in this study, that a risk score developed in one population performs poorly when applied to other populations of different ethnic background.

Although there may be issues with age ascertainment and measuring waist circumference and blood pressure as discussed in chapter 6 on page 125, the risk score is simple enough for use by health workers, and can be used both at the health facility level and during community outreach programs. Majority of people would be aware of their age, but the challenge remains with those that have poor literacy and the elderly, but often their age is estimated using major life events such as the age of their children, major country events like independence etc. Health care workers can be trained on proper measurements of

waist circumference, and also blood pressure measurement form part of routine health check at the health facilities.

At this stage when community wide screening for diabetes is not recommended, I see this risk score being useful in primary health care setting where services for diagnosis may be unavailable; hence it can be used to identify individuals at high risk of diabetes that can be referred to the next level of care for confirmatory diagnosis and further management. However it should be acknowledged that the effectiveness of the screening will be dependent on the availability of a proper resources infrastructure to support the screening program, which is discussed in detail in chapter 3, 6, 7 and 8.

During implementation of such a screening program, there will be individuals that will be detected with prevalent diabetes which present opportunity for secondary prevention i.e. early treatment of hypertension, blood glucose control, treatment with lipid lowering agents etc. to prevent micro and macrovasular complications and also management of prevalent complications to prevent disability (tertiary prevention). Diabetes screening also identifies individuals at high risk of diabetes who may benefit from primary prevention programs, this particularly presents a challenge especially in Sub-Saharan Africa where there not yet systems or there may be little resources both technical know-how and budgetary available to implement such interventions. There will be need to engage with policy makers in order to ensure evidence based decision making in developing and implementing plans to strengthen care for diabetes and other cardiovascular diseases.

The study was limited in several ways. First the study used secondary data from previous diabetes studies. Not all the variables were assessed the same way therefore some of the variables could not be used to derive the score. Also the family history variable was lacking in some of the data sets therefore was not included as a predictor variable. Not all variables were present to enable validation of all existing scores and, as a result, some scores could not be validated. The diagnostic methods for diabetes varied across studies which could be a source of bias and makes it difficult to compare the various risk scores. In addition, a completed case analysis was undertaken to deal with missing data this could also potentially bias the findings of this study especially if the data was not missing at random.

Secondly, the data that were used to validate the clinical utility of the new score were based on a convenience sample so caution must be applied as the findings might not be transferable to the Tanzanian population.

This study was focused on determining prevalent undiagnosed diabetes; more research is needed to validate the score across other African settings and also to study the feasibility of applying the score for opportunistic screening in a clinical setting and to investigate the issues related to who to screen, how should the score be applied, whether be filled by nurses or clinicians attending patients, issues related to acceptability by both the health workers and patients, resources needed and identify challenges of implementation as a whole and also the resources required to implement such as screening program.

This type of evaluation could not be undertaken during the present study because of time and other resource limitations. Further research will also be needed to evaluate the process and also the outcome of screening in terms of reducing the unfavourable diabetes outcomes. This research has also thrown up many questions that need further investigations such as the need to explore the score's capacity to predict incident diabetes and in predicting pre diabetes which are essential components in identifying individuals at high risk of diabetes targeted for primary prevention interventions.

What this study adds is that I have developed the first ever diabetes risk score for Africa. This score performed better compared to other available risk scores developed from developed countries as discussed in detail in chapter 7 on page 128 .

The policy implications of this study is that results of this support the idea that there is no universal score that is applicable to all but rather it is possible to have a risk score that cuts across different settings; instead of having a plethora of new scores efforts should be directed towards validating and adapting existing, simple risk scores that are relevant across different settings and; are using predictor variables that are not culturally specific and; those that can be consistently and accurately measured. The choice of the risk score to be used should be guided by the local needs. Before adapting a score for use, it should be validated and re calibrated if necessary to suit the local population.

Diabetes screening to identify high risk individuals to be directed for proper interventions has to be organised in a systematic manner for it to be cost effective and countries need to develop their screening strategies based on resources available. Facts to support universal screening for diabetes are unclear but available evidence supports screening of

individuals at high risk of diabetes by opportunistic screening (chapter 3). Diabetes risk scores are a could be a feasible approach as an initial screening tool to reduce the number of individuals that would require a confirmatory blood test which tend to be more expensive and unavailable, for example in rural African settings.

Appendix

Appendix 1 Selected Publications, Presentations and Certificates of Attendance to Conferences and Seminars

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International Diabetes Federation

Review

Screening for hyperglycemia in the developing world: Rationale, challenges and opportunities

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ABSTRACT

Background: The prevalence of diabetes and prediabetes are increasingly high in developing countries, where detection rates remain very low. This manuscript discusses the rationale, challenges and opportunities for early detection of diabetes and prediabetes in developing countries.

Methods: PubMed was searched up to March 2012 for studies addressing screening for hyperglycemia in developing countries. Relevant studies were summarized through key questions derived from the Wilson and Junger criteria.

Results: In developing countries, diabetes predominantly affects working-age persons, has high rates of complications and devastating economic impacts. These countries are ill-equipped to handle advanced stages of the disease. There are acceptable and relatively simple tools that can aid screening in these countries. Interventions shown to be cost-effective in preventing diabetes and its complications in developed countries can be used in screen-detected people of developing countries. However, effective implementation of these interventions remains a challenge, and the costs and benefits of diabetes screening in these settings are less well-known. Implementing screening policies in developing countries will require health systems strengthening, through creative funding and staff training.

Conclusions: For many compelling reasons, screening for hyperglycemia preferably targeted, should be a policy priority in developing countries. This will help reorient health systems toward cost-saving prevention.

Contents

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International Diabetes Federation

Review

Risk scores based on self-reported or available clinical data to detect undiagnosed Type 2 Diabetes: A systematic review

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ABSTRACT

Objective: To systematically review published primary research on the development or validation of risk scores that require only self-reported or available clinical data to identify undiagnosed Type 2 Diabetes Mellitus (T2DM).
Methods: A systematic literature search of Medline and EMBASE was conducted until January 2011. Studies focusing on the development or validation of risk scores to identify undiagnosed T2DM were included. Risk scores to predict future risk of T2DM were excluded.
Results: Thirty-one studies were included; 17 developed a new risk score, 14 validated existing scores. Twenty-six studies were conducted in high-income countries. Age and measures of body mass/fat distribution were the most commonly used predictor variables. Studies developing new scores performed better than validation studies, with 11 reporting an AUC of >0.80 compared to one validation study. Fourteen validation studies reported sensitivities of <80%. The performance of scores did not differ by the number of variables included or the country setting.
Conclusions: There is a proliferation of newly developed risk scores using similar variables, which sometimes perform poorly upon external validation. Future research should explore the recalibration, validation and applicability of existing scores to other settings, particularly in low/middle income countries, and on the utility of scores to improve diabetes-related outcomes.

Contents

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7th World Congress
on Prevention of Diabetes
and its Complications
11 to 13, November 2012
Madrid, Spain

"Making Prevention a Reality"

CERTIFICATE

To whom it might concern

Mary Mayige

has presented the oral communication:

"Diabetes risk score for undiagnosed diabetes in African populations"

7th World Congress on Diabetes Prevention and its Complications

that was held in Madrid from November 11th to 13th 2012

Madrid, November 13th, 2012

Professor Jaakko Tuomilehto

Dr. Rafael Gabriel

THE AFRICAN D I A B E T E S CONGRESS
1st Scientific Sessions
25 - 28 July 2012
Arusha International Conference Centre, Arusha, Tanzania

Monday, 30th July, 2012

Dr. Mary Mayinge
TANZANIA

Dear Dr. M.Mayinge,

On behalf of the Organizing Committee, 1st Scientific Sessions, African Diabetes Congress, we would like to thank you for generously giving your time to serve as speaker at the African Congress and / or Satellite events, which took place in Arusha, Tanzania, 20 – 28 July 2012.

Your presentation added great value to the session's content and contributed meaningfully to the overall success of the Congress and Satellite Events.

The Congress was a unique opportunity to discuss ambitions, priorities and actions for change in diabetes and non-communicable diseases within sub-Saharan Africa. The weeklong events brought together more than 600 delegates from different fields across 32 countries in the sub-Saharan African region and abroad, who joined the call for united action and cooperation.

We believe that the relationship and network that formed as a result of this Congress will contribute to generating new, innovative and sustainable solutions for Africa and indeed the global agenda on the prevention and management of diabetes and other non-communicable diseases.

As one of the distinguished speakers, we particularly hope that this offered an opportunity for you to promote your work and identify new partners, and hope that it offers a further opportunity to lobby others and join us in future African Diabetes Congresses.

Sincerely,

Dr. Silver Bahendeka

Dr. Kaushik Ramaiya

On Behalf of the Organising Committee
1st Scientific Sessions, African Diabetes Congress, 2012 Arusha, Tanzania

Newcastle University

Institute of Health & Society

DERIVATION AND VALIDATION OF A RISK SCORING SYSTEM FOR IDENTIFICATION OF UNDIAGNOSED TYPE 2 DIABETES FOR TANZANIA AND OTHER AFRICAN POPULATIONS

Mary Mayige[1,2] (mary.mayige@ncl.ac.uk)

Nigel Unwin[1], Eugene Sobngwi[1], Richard McNally[1], Richard Walker[1]

[1] Institute of Health and Society, Newcastle University, [2] National Institute for Medical Research, Tanzania

Background

- Diabetes Mellitus is condition that is characterised by chronic hyperglycaemia which results from defects of insulin secretion action or both.
- Two main types of diabetes, type 1 and 2.
- Pathogenesis of type 2 diabetes is linked to modifiable lifestyle risk factors e.g. diet and physical activity.
- Burden of diabetes is increasing worldwide. In Africa, the total number of diabetes cases is estimated to be 12.1 million[1].
- Prevalence of diabetes in Africa is estimated to be 3.2% varies across countries (fig1). In some countries up to 80% of people with diabetes are undiagnosed[1].
- Studies have shown that prevention of diabetes and its complications is possible; the outcomes are better and interventions are more cost effective if treatment is initiated early[2].
- Early identification of individuals at high risk is important.
- The QDS is an example of a risk score tool developed in the UK for predicting individual's risk of developing diabetes based on their profile of certain risk factors[3].

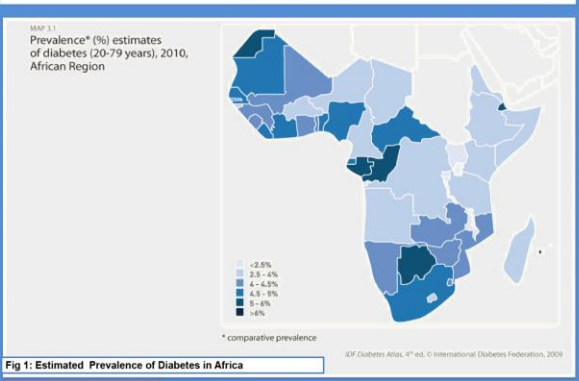

Fig 1: Estimated Prevalence of Diabetes in Africa

The Problem

- Diabetes is an important problem in Tanzania.
- Cases are often diagnosed late and with complications .
- Secondary prevention of diabetes is possible with blood glucose, blood pressure and lipids control.
- Lack of diagnostic facilities contribute to high rates of undiagnosed cases.
- Risk score tools are a feasible option to identify those at high risk of diabetes and identifying undiagnosed diabetes.
- No tool is currently available for the African population.

Objectives

- To derive a diabetes risk scoring tool from data sets of studies done in Tanzania and African populations.
- To validate the risk score derived in an independent sample within the data set.
- To validate the risk score in a clinical setting.
- To examine the current diagnostic pathway for diabetes and compare the characteristics of the newly diagnosed with those identified by the tool.
- To evaluate the work load, yield and comment on the cost of applying the tool in a clinical setting.

Methods

The study will have 3 phases;

Phase 1: Deriving the risk scores

Risk scores will be developed by regression analysis of the risk factors from data sets form population based diabetes surveys. ß coefficients from the analysis will be used to compute weightings for score.

Phase 2: Validating the score in an Independent Sample of the data set

The score will be validated in the data set and its performance in detecting undiagnosed diabetes evaluated in terms of sensitivity, specificity, positive and negative predictive values. Receiver Operating Characteristic Curve will be plotted and the Area under the Curve and the cut off points for diagnosis will be determined.

Phase 3: Evaluation of the clinical usefulness of the tool

The tool will be tested in 1200 patients, aged 35-64yrs attending outpatient clinics in district hospitals in Dar es Salaam, Tanzania. The patients will be subjected to a risk score questionnaire, physical measurements and a fasting blood glucose test

The patients diagnosed by the tool will undergo further tests at the diabetes clinic as part of their diagnostic workup.

The tests include:

- A repeat fasting glucose measure to confirm diagnosis
- Eye examination (fundoscopy)
- Urine protein
- Renal Function Tests (Blood Urea and Creatinine)
- Blood Cholesterol Measurements (HDL, LDL and Triglycerides)
- Glycated Haemoglobin measurement (HBA1c)
- Echocardiogram and Rose Angina Questionnaire
- Foot examination.

The tool will then be evaluated in terms of its capacity to identify undiagnosed diabetes, the cost, additional work load , the yield and the patient characteristics as compared to the normal diagnostic pathway. Patient characteristics will be compared using the results of the above tests which will be collected from the diabetes clinic registry.

Conclusion

The developed tool will be simple enough to be used in health care settings where blood glucose measurements are unavailable as an initial screening tool to identify high risk patients that can then be referred to the higher levels of care for further testing.

References

1-Diabetes atlas, Fourth Edition.2009, International Diabetes Federation, Brussels.

2- Kahn, R. Et al, Age at Initiation and Frequency of Screening to Detect Type 2 Diabetes: A cost Effective Analysis. The Lancet 375(9723), p 1365-1374, 2010.

3-Hippisley-Cox, J. et al, Predicting risk of type 2 diabetes in England and Wales: Prospective Derivation and Validation of QDS core. BMJ,2009.338:p.880.

EACCME

European Accreditation Council for Continuing Medical Education

CERTIFICATE

6th World Congress on Prevention of Diabetes and its Complications

Dresden, Germany (8 – 11 April 2010)

has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide the following CME activity for medical specialists.

6th World Congress on Prevention of Diabetes and its Complications is designated for a maximum of, or up to 21 European CME credits (ECMEC's).

Dr. Mary Mayige

United Kingdom

Each medical specialist should claim only those credits that he/she actually spent in the educational activity.
The EACCME is an institution of the European Union of Medical Specialists (UEMS), www.uems.net.
ECMEC's are recognized by the American Medical Association towards the Physician's Recognition Award (PRA).
To convert ECMEC's credit to AMA PRA category I credit, please contact the AMA.

Clare College, Cambridge, UK

3rd – 9th July 2011

This is to certify that

Mary Mayige

participated in the

11th WHO/IDF/EASD Cambridge Seminar on the Epidemiological and Public Health Aspects of Diabetes Mellitus

Dr Nita Forouhi and Professor Nicholas Wareham

Sponsors: EASD, InterAct, International Diabetes Federation, World Health Organization

Appendix 2 The Scoring System used for the QUADAS Tool to Assess Quality of Studies included in the Review of Diabetes Risk Scores

QUADAS Item	Y =Yes, N =No, U =Unclear
1. Was the spectrum of patients' representative of the patients who will receive the test in practice?	Y- participants enrolled reflect those affected by the condition in practice
	N- participants enrolled does not reflect those affected by the condition in practice
	U-if the source or characteristics of participants is not adequately described
2. Were selection criteria clearly described?	Y-participant selection criteria adequately described
	N-patient selection criteria not clearly reported
	U- if insufficient information is given to permit judgement
3. Is the reference standard likely to correctly classify the target condition?	Y- if OGTT, FBG or HbA1c is used to as reference standard
	N-if another test is used
	U- if insufficient information is given to permit judgement
4. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?	Y-if all participants received both index(risk score) and reference test
	N-if not all participants received both index and reference test
	U- if insufficient information is given to permit judgement
5. Did patients receive the same reference standard regardless of the index test result?	Y-if the same reference test was used in all participants
	N-if different reference tests are used depending on index test
	U- if insufficient information is given to permit judgement
6. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	Y-if OGTT , HbA1c or FBG is the reference test
7. Was the execution of the index test described in sufficient detail to permit replication of the test?	Y- if details of the process of derivation and validation of the score (the index tests) are provided
	N-if no details of the index test
	U- if insufficient information is given to permit judgement
8. Was the execution of the reference standard described in sufficient detail to permit its replication?	Y- if details of execution of reference tests are provided
	N-if no details of execution of the reference test
	U- if insufficient information is given to permit judgement

9. Were uninterruptable/ intermediate test results reported?	Y-if the number of patients that have undergone the tests matches the number reported in results
	N- if the number of patients that have undergone the tests does not matches the number reported in results
	U-if insufficient information is given to permit judgement
10. Were withdrawals from the study explained?	Y-if there are no participants excluded from the analysis, or if the exclusions are adequately explained
	N-if there are unexplained exclusions from the study
	U-if insufficient information is given to permit judgement

Appendix 3 Patient Consent Forms (English and Swahili Versions)

PATIENT CONSENT FORM

Identification number: _____

Title of project: DERIVATION AND VALIDATION OF A RISC SCORING SYSTEM FOR IDENTIFICATION OF UNDIAGNOSED DIABETES FOR TANZANIA AND OTHER AFRICAN POPULATIONS

Name of researcher; Dr Mary Mayige

I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that my participation is voluntary and that am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected

I agree to have my height and weight, waist and hip circumference measured and my Blood pressure checked and recorded

I agree to complete a short questionnaire to check my risk for diabetes

I agree to fasting blood glucose measurements

I understand that the information collected in the study may be viewed by other members of the research team [in addition to those named] for the purposes of quality control and by Research Governance auditors.

I agree to take part in this study

Name of Patient	Date	Signature
Researcher	Date	Signature

_____

FOMU YA RIDHAA KUSHIRIKI KWENYE UTAFITI

*Namba ya utambulisho:*_____

Jina la Utafiti: DERIVATION AND VALIDATION OF A RISC SCORING SYSTEM FOR IDENTIFICATION OF UNDIAGNOSED DIABETES FOR TANZANIA AND OTHER AFRICAN POPULATIONS

Majina ya mtafiti; Dr Mary Mayige

Nakubali kwamba nimesoma/nimesomewa na kuelewa maelezo yaliyotolewa kuhusu utafiti huu. Nimepata fursa ya kuchambua maelezo yaliyotolewa na kuuliza maswali. Nimeridhika na maelezo niliyopata.

Naelewa kuwa ushiriki wangu ni wa hiari na nina haki ya kujitoa ushiriki kwenye utafiti huu muda wowote bila kupoteza haki zangu au upotevu wa faida yeyote ninayotakiwa kupata

Nakubali kufanyiwa vipimo vilivyotajwa kama kupima urefu, upana wa kiuno, uzito na shinikizo la damu

Nakubali kufanyiwa kipimo cha kiwango cha sukari kwenye damu

Nakubali kujaza dodoso fupi ambalo lina maswali yanayolenga kutathmini uwezekano wangu wa kuwa na kisukari

Naelewa kuwa taarifa zitakazochukuliwa kwenye utafiti huu zinaweza kuonwa na watu mbali mbali ambao wanahusika na utafiti huu [tofauti na waliotajwa hapo juu] kwa ajili ya kutatmini kiwango cha utafiti huu na waangalizi wa viwango vya tafiti.

Nakubali kushiriki kwenye utafiti huu

Jina la mgonjwa	Tarehe	Sahihi
Jina la mtafiti	Tarehe	Sahihi

_____

Appendix 4 Patient Information Sheets (English and Swahili Versions)

PARTICIPANT INFORMATION SHEET

Introduction

Greetings! This form contains information about the study on derivation and validation of a tool to detect undiagnosed diabetes. To be sure you understand the study we ask you to read this form (or have it read to you). The form may contain some words that you do not understand, please ask us to explain anything that you may not understand.

Reason for the research

This study is being conducted in order to develop a simple tool that can be used to detect undiagnosed diabetes in settings where blood glucose measurements may not be feasible or available

General Information about the study

We are inviting people like you between ages of 35 to 64 who are attending general outpatient clinics at the district hospital. That is the age where diabetes is common.

Your part in the research

If you agree to participate in this study:

You will be asked to complete a questionnaire that is meant to assess your individual risk for diabetes. Your height and weight, waist measurement and blood pressure will be checked.

Identifying information will be collected from you during this interview, but all information will be kept confidential

You will also be given an appointment for a blood sugar test that involves the following; you will be required not to eat or drink anything 8 hours before the test, you will be given morning appointments for convenience and you will be provided with some refreshments after the test. The blood test will be a finger prick. You will be reimbursed your transport cost however this is restricted to public transportation

Confidentiality

I assure you that all the information collected from you will be kept confidential. Only people working in this research study will have access to the information. We will be compiling a report, which will contain responses from several diabetic patients without any reference to individuals.

Risks

You will be asked questions about factors that are associated with the risk of diabetes. You may refuse to answer any particular question and may stop the interview at any time if you feel uncomfortable. Taking part will also take up some of your time. You will have to return another day for the fasting glucose test

Rights to Withdraw and Alternatives

Taking part in this study is completely your choice. If you choose not to participate in the study or if you decide to stop participating in the study you will not get any harm. You can stop participating in this study at any time, even if you have already given your consent. Refusal to participate or withdrawal from the study will not involve penalty or loss of any benefits to which you are otherwise entitled.

Benefits

As a result of you taking part in the study we might identify a way if improving your healthcare, you will be given feedback on your health status and information how to reduce your risk of getting diabetes. Even if this is not the case the information that you give us will help us to ensure that good quality health care is provided to other people like you. The information collected will allow us to develop and refine a tool that predicts diabetes so it is more useful for populations like our own.

In Case of Injury

We do not anticipate that any harm will occur to you or your family as a result of participation in this study

Who to contact

If you ever have questions about this study, you should contact the study Coordinator or the Principal Investigator, Rd. Mary .T. Mayige, National Institute for Medical Research, P.O.Box 538 Tukuyu. (Tel.0713255456). If you ever have questions about your rights as a participant, you may contact NIMR ethics review committee, P.O.Box 9653, Dar es Salaam, (Tel. 022 2121400) , and Dr Eugene Sobngwi, Newcastle University, Institute of Health and Society, Newcastle upon Tyne,NE2 4AX, United Kingdom who is the supervisor of this study (Tel. +44 (0)191 222 8897).

FOMU YA MAELEZO YA UTAFITI

Utangulizi

Habari! Fomu hii ina maelezo juu ya utafiti unaohusu tathmini ya upimaji wa kisukari. Lengo la utafiti huu ni kuainisha jinsi ya kuwatambua wagonjwa wa kisukari bila kutumia kipimo cha damu. Kabla ya kuanza kushiriki tunaomba usome (au tukusomee) maelezo yaliyoko kwenye fomu hii. Fomu hii inaweza kuwa na maneno ambayo ni magumu kwako, kwa hiyo tafadhali usisite kuomba ufafanuzi kwa maneno ambayo hutayaelewa.

Malengo ya Utafiti

Utafiti huu una lengo la kuanisha jinsi ya kuwatambua watu wenye tatizo la kisukari bila kufanya kipimo cha sukari kwenye damu. Ugunduzi huu utasaidia kugundua wagonjwa wengi zaidi wa kisukari kwenye maeneo ambayo kipimo cha damu hakipatikani au hakiwezi kufanyika

Taarifa kuhusu utafiti huu

Tunakaribisha wagonjwa mbalimbali wenye umri kati ya miaka 35 na 64 wanaohudhuria cliniki mbalimbali katika hospitali za wilaya mkoani Dar es Salaam. Ugonjwa wa kisukari huwapata zaidi watu walio katika umri huu.

Nini kitatokea iwapo utakubali kushiriki

Ukikubali kushiriki katika utafiti huu yafuatayo yatatokea:

1. Utaombwa kujaza dodoso ambalo lina maswali yanayolenga kutathmini uwezekano wako wa kuwa na kisukari. Pia utapimwa urefu na uzito, upana wa kiuno na shinikizo la damu

2. Tutakusanya taarifa chache za utambulisho ambazo zitatunzwa kwa usiri.

3. Pia utapangiwa siku ya kurudi kwa ajili ya kupima sukari kwenye damu. Kipimo hiki kitahitaji: usile au kunywa kitu chochote masaa nane kabla ya kutolewa damu, utapewa ahadi ya mapema asubuhi ili iwe rahisi kufanyiwa kipimo kabla ya chai. Utatolewa damu kwenye kidole kwa ajili ya kupima wingi wa sukari. Baada ya

kuchukuliwa kipimo utapewa kitu kidogo cha kula . Pia utarudishiwa nauli ya dala dala uliyotumia kurudi hospitali kwa ajili ya kipimo.

Usiri

Tunapenda kukuhakikishia kwamba taarifa zote utakazotupatia zitakuwa ni siri, ni watu wanaofanya kazi katika utafiti huu tu ndio wanaweza kuziona taarifa hizi. Tutajumuisha ripoti ambayo itakua na majibu kutoka kwa wagonjwa kadhaa bila kuweka taarifa zao za utambulisho.

Madhara

Utaulizwa maswali juu ya masuala ambayo yanaweza kukusababishiakupata kisukari. Baadhi ya maswali yanaweza kukukera kidogo.. Unao uwezo wa kukataa kujibu swali lolote na pia unaweza kusitisha ushiriki wako kwenye utafiti huu wakati wowote. Kushiriki kwenye utafiti huu kutatumia muda wako, kwa sababu utahitajika kurudi tena hospitali kwa ajili ya kipimo cha damu.

Haki ya kujitoa

Kushiriki katika utafiti huu ni hiyari yako. Unaweza kutokushiriki au kuamua kusitisha ushiriki wako bila kupata madhara yoyote. Unaweza kusitisha kushiriki katika utafiti huu muda wowote hata kama ulisharidhia kushiriki. Kukataa kushiiriki au kujitoa katika utafiti hakutaambatana na adhabu yoyote au upotevu wa faida yoyote unayotakiwa kupata.

Faida

Faida ya kushiriki kwako katika utafit huu ni pamoja na wewe binafsi kupata maelezo ya yatakayokusaidia kujua hali yako ya kiafya na jinsi ya kuweza kujikinga na matatizo yanayoweza kukusababishia kisukari au kujikinga na madhara zaidi yanayotokana na kisukari kwa wale watakaogundulika kuwa na kisukari. Vilevile hata kama wewe binafsi hutakuwa na tatizo la kisukari taarifa utakazotupatia kwakushiriki kwako zitasaidia kuboresha huduma kwa wagonjwa wa kisukari na taarifa itakayotokana na utafiti huu itasaidia katika kugundua njia ya kutambua wagonjwa wa kisukari kwenye jamii yetu bila kulazimika kuchukua vipimo vya damu.

Endapo Utadhurika

Hatutegemei madhara yoyote kwako au kwa familia yako kwa kushiriki kwako katika utafiti huu.

Watu wa kuwasiliana nao

Kama una maswaIi zaidi kuhusu utafiti huu unaweza kuwasiliana na mratibu mkuu wa mradi, Dr. Mary .T. Mayige, Taasisi ya Utafiti wa Magonjwa ya Binadamu (NIMR), S.L.P 538 Tukuyu (Simu. no. 0715255456). Kama utakuwa na maswali yoyote kuhusu haki zako kama mshiriki unaweza kuwasiliana na kamati ya taifa ya maadili ya utafiti , S.L.P 9653 , Dar es Salaam (Simu namba: 0222121400) au Dr Eugene Sobngwi wa Chuo Kikuu cha Newcastle (Newcastle University), Institute of Health and Society, Newcastle upon Tyne,NE2 4AX, United Kingdom ambaye ni msimamizi wa utafiti huu (Simu nambari. +44 (0)191 222 8897)

Appendix 5 Ethics

THE UNITED REPUBLIC OF
TANZANIA

National Institute for Medical Research
P.O. Box 9653
Dar es Salaam
Tel: 255 22 2121400/390
Fax: 255 22 2121380/2121360
E-mail: headquarters@nimr.or.tz

Ministry of Health and Social Welfare
P.O. Box 9083
Dar es Salaam
Tel: 255 22 2120262-7
Fax: 255 22 2110986

NIMR/HQ/R.8a/Vol. IX/972

22nd June 2010

Dr Mary Mayige
NIMR Tukuyu
P O Box 538 TUKUYU
Mbeya

CLEARANCE CERTIFICATE FOR CONDUCTING MEDICAL RESEARCH IN TANZANIA

This is to certify that the research entitled: Derivation and Validation of a Simple Risk Score for Detection of Undiagnosed Diabetes for Tanzania and Other African Populations, (Mayige M *et al)*, has been granted ethics clearance to be conducted in Tanzania.
The Principal Investigator of the study must ensure that the following conditions are fulfilled:

1. Annual Progress report is submitted to the Ministry of Health and the National Institute for Medical Research, Regional and District Medical Officers.
2. Permission to publish the results is obtained from National Institute for Medical Research.
3. Copies of final publications are made available to the Ministry of Health & Social Welfare and the National Institute for Medical Research.
4. Any researcher, who contravenes or fails to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine. NIMR Act No. 23 of 1979, PART III Section 10(2).
5. Approval is for one year: 22nd June 2010 to 21st June 2011.

Name: Dr Mwelecele N Malecela

Signature

ACTING CHAIRPERSON
MEDICAL RESEARCH
COORDINATING COMMITTEE

Name: Dr Deo M Mtasiwa

Signature

CHIEF MEDICAL OFFICER
MINISTRY OF HEALTH, SOCIAL WELFARE

CC: RMO
DMO

16 May 2011

Mary Mayige
PhD Student
Institute of Health and Society

Faculty Research Strategy Office
Faculty of Medical Sciences

Newcastle University
The Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH United Kingdom

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Mary

Title: Derivation and Validation of a Risk Scoring System for Identification of Undiagnosed Diabetes for Tanzania and Other African Populations
Application No: 00436/2011
Expected Start and end Dates: January 2011 to December 2011

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of the changes to your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: 00436/2011. If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation.*

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee.*

Best wishes,

Yours sincerely

M. Holbrough

Marjorie Holbrough
On behalf of Faculty Ethics Committee

cc.
Professor T E Cawston, Dean of Research
Ms Lois Neal, Assistant Registrar (Research Strategy)
Dr Eugene Sobngwi
*Please refer to the latest guidance available on the internal Newcastle Biomedicine web-site.

tel :+44 (0) 191 222 7073
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frsg.medicalsciences@ncl.ac.uk
www.ncl.ac.uk

Appendix 6 Field Manual

Derivation and Validation of a Simple Tool for Detection of Undiagnosed Diabetes

Field Manual

Investigator: Mary Mayige

Supervisors: Dr Eugene Sobngwi

Prof Richard Walker

Dr Richard Mcnally

Introduction

Diabetes and its associated conditions is an increasing problem in the country and cause a great burden on the country's health system. Many diabetes patients remain undiagnosed and as a result present to the hospitals at late stages of the disease. This study is being undertaken as part of a study to develop and test a simple tool for identifying undiagnosed diabetes in clinical and non clinical settings. The protocol has been developed to standardise data collection procedures and for training of research assistants and also to provide a documentation of the process of data collection.

Methods and Design

Aims and objectives

The aim of this phase of the project is to;

1. validate the risk score in a clinical setting
2. evaluate the yield and
3. Comment on the cost of applying the tool in a clinical setting

Study sample

Inclusion criteria: Patients 35 to 64 years invited to participate in the study at district hospitals from various areas of Dar es Salaam

Exclusion criteria: Age <35 and >64 years

Sample size

The total estimated sample size is at least 1200. A sample of 200 with and 1000 without disease is needed to achieve a minimal standard error of the parameter estimate of tool performance.

Data collection

Assessment of diabetes risk

- Selected patients are subjected to the risk score questionnaire which is derived from the first part of the study and a general diabetes questionnaire

Physical measurements include[1];

- Weight; measured using a standard calibrated portable weighing scale while patient is barefoot and wearing light clothing
- Height; measured while patient is barefoot using a standard stadiometer
- Blood Pressure; measured using a standard electronic Blood Pressure machine
- Waist and hip Circumference; measured using a flexible tape and categorised using WHO guidelines
- Fasting blood glucose measurements;

An appointment will be given for fasting blood glucose measurements, participants will be asked to fast for a minimum of 12 hours. Blood sample is taken by a finger prick, and analysed using a portable glucometer. Hyperglycaemia will be classified according to the standard WHO criteria. Patients will be reimbursed transport costs for the additional visits. Patients contact details should be taken to facilitate follow up for the fasting glucose measurements. The participants will be classified as a loss to follow up after at least three failed follow up attempts.

Yield and the Cost of using the Score

The yield of patients with undiagnosed diabetes will be compared to those diagnosed through the routine diagnostic pathway. Those classified as diabetic from the blood glucose measurements should be referred to the diabetic clinic. These patients will have to undergo further tests. These include a repeat fasting glucose to confirm diagnosis, eye exam (fundoscopy), urine protein using rapid tests(uristics) and further urine analysis if resources allow, foot examinations, ECG and venous blood is taken for cholesterol , renal function tests (blood creatinine) and if possible glycated haemoglobin measurements. To document resources required to carry out the screening, all materials and time taken to complete the risk score and give feedback should be recorded for each of the participant.

Research Assistants

Research assistants are to be recruited from the sites to assist with patient recruitment, interviews, physical and laboratory examination .The research assistants will have specific roles which includes; registration and questionnaire administration, physical as well as

[1] According to the WHO STEPS Guidelines

laboratory measurements. These should preferably be nurses, medical assistants and laboratory technicians. Research assistants should be adequately trained before beginning the research activities. The team should be aware of infection prevention guidelines and procedures especially those involved with taking blood samples from patients, Refer to the National infection prevention and control guidelines for health care services in Tanzania.

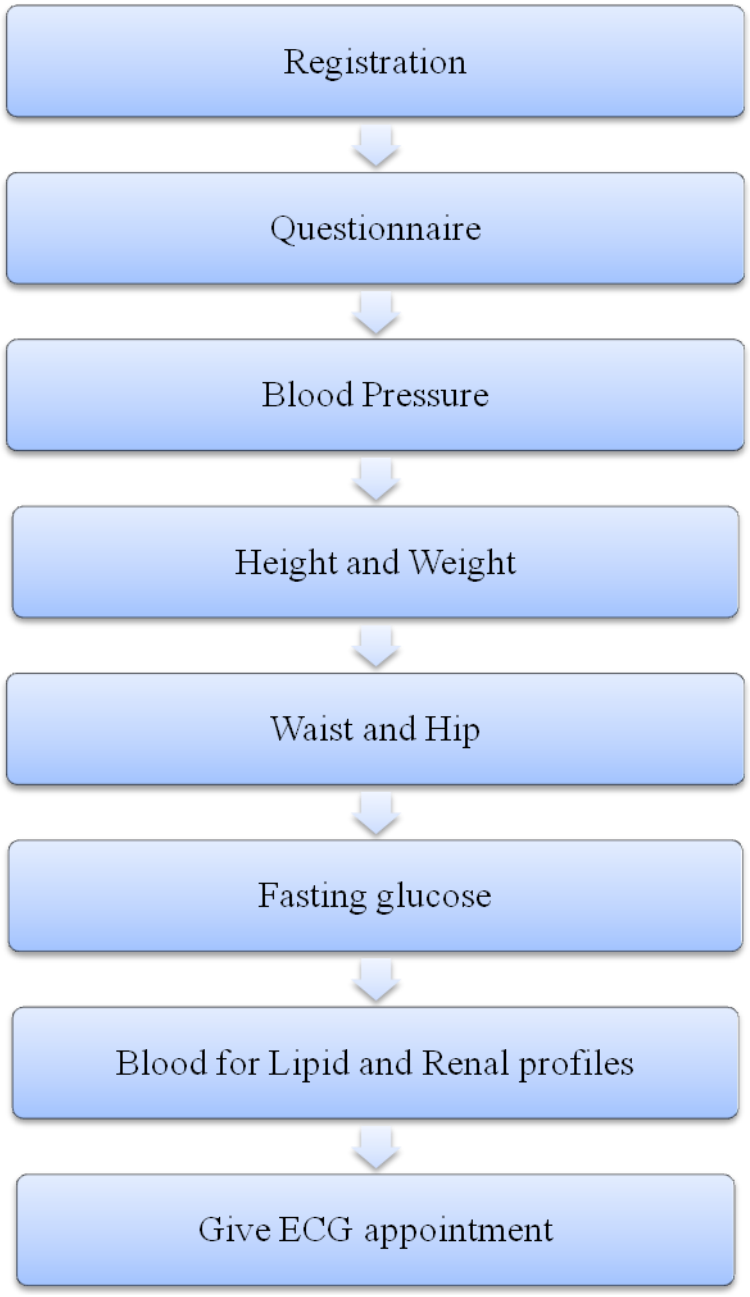
Setting

The study sites include Ilala, Temeke and Mwananyamala District Hospital; it is the responsibility of the study PI to liaise with the hospital administration to obtain an appropriate setting/ room that will allow interviews and the clinical examination procedures to be carried out.

Patient Recruitment Procedures

Participants will be invited to participate from different areas of Dar es Salaam, invitations to participate will be sent out to different social gatherings e.g. churches and mosques, advertisement for study will also be placed at busy areas.

Summary of Patient Flow and Activities



Registration

This should take place in a quiet place, with a table and chairs

Greet the subject

Determine eligibility based on the stated inclusion/ exclusion criteria

Provide information about the study (refer to the study information leaflet)

If the subject agrees to participate, take the participant through the informed consent form make sure they have understood what has been explained to them before asking them to sign the form

Add the patient to the register and prepare for administering questionnaire

Completing the Questionnaire

Ask the participant to complete the study questionnaire

Start with administering the Risk Score and do not forget to record start and finish time

Follow with the survey Questionnaire, do not repeat the questions, fill in repeating questions with information from the risk score

Questions should be asked in a standard manner using Kiswahili and record answers legibly using a pen in appropriate spaces provided. Do not leave any question blank.

Follow the specific instructions for completing the different items in the questionnaire

Direct the patient to the person responsible for physical measurements

Physical Measurements

The following physical measurement will be done;

Taking Blood Pressure and Recording Heart Rate

Measuring Height

Measuring Weight

Measuring Waist Circumference

Measuring Hip Circumference

Physical Measure	Unit of Measurement
Systolic blood pressure(SBP)	mmHg
Diastolic blood pressure (DBP)	mmHg
Height	Cm
Weight	Kg
Body mass index (BMI)	Kg/m^2
Waist circumference	Cm
Hip circumference	Cm
Heart rate	Beats/minute

Sequence of tests

The physical measurements should be taken from the participant in the following order:

1. Blood pressure and heart rate
2. Height
3. Weight
4. Waist circumference
5. Hip circumference.

Equipments required for tests:

Please prepare the following the physical measurement station

blood pressure monitor and appropriate cuff sizes= OMRON blood pressure machines will be provided

height measuring board;

weighing scales;

tape measure;

pen;

chair or coat rack for participant's clothes;

curtain or screen to provide privacy if no private area is available for taking measurement

Measuring Blood Pressure and Heart Rate

Equipment: OMRON digital blood pressure machine

Preparing the patient: Ask the participant to sit quietly and rest for 15 minutes with his/her legs uncrossed. If the subjects had been seated during and after questionnaire administration,

arrangements should be made to make sure that they move only a short distance to the blood pressure station so that blood pressure can be measured without having to wait for 15 minutes.

Measurements: See instructions below and Refer to the manufacturer's instructions for measuring blood pressure. Three blood pressure measurements and pulse rate should be taken. During data analysis the mean of the second and third readings will be calculated. Make the patient rest for three minutes between each of the readings.

record your Interviewer ID (if not already filled in) in the participant's instrument;

after each of the three measurements, record the results in the participant's instrument;

check that all readings are correctly filled in the instrument;

inform the participant on the blood pressure readings only after the whole

The instructions below apply to the use of an OMRON blood pressure monitor.

Applying the OMRON cuff; follow the steps below to select an appropriate size and apply the cuff:

1. Place the left arm* of the participant on the table with the palm facing upward.
2. Remove or roll up clothing on the arm.
3. Select the appropriate cuff size for the participant
4. Position the cuff above the elbow aligning the mark ART on the cuff with the brachial artery.
5. Wrap the cuff snugly onto the arm and securely fasten with the Velcro.

Note: The lower edge of the cuff should be placed 1.2 to 2.5 cm above the inner side of the elbow joint.

6 Keep the level of the cuff at the same level as the heart during measurement.

Taking the measurement with an OMRON

Follow the instructions below to take the blood pressure measurement:

1. Switch the monitor on and press START
2. The monitor will start measuring when it detects the pulse and the "heart" symbol will begin to flash. The systolic and diastolic blood pressure readings should be displayed within a few moments

(systolic above and diastolic below).

3. Record the reading in the participant's instrument.

4. Switch the monitor off, but leave the cuff in place.

5 .Wait three minutes, then repeat steps 1-4 two more times.

Measuring Height

Equipment: Portable stadiometer

Preparing the patient: Ask the participant to remove their:

Footwear (shoes, slippers, sandals, etc)

Head gear (hat, cap, hair bows, comb, ribbons, etc). Note: If it would be insensitive to seek removal of a scarf or veil, the measurement may be taken over light fabric.

Taking the measurement

Follow the steps below to measure the height of a participant:

Ask the participant to stand facing forward.

Ask the participant to stand with:

feet together

heels against the wall

knees straight.

Ask the participant to look straight ahead and not tilt their head up.

Make sure eyes are the same level as the ears.

Lower the measuring plate gently down onto the head of the participant and ask the participant to breathe in and stand tall.

Read the height in centimetres at the exact point.

Ask the participant to step away.

Record the height measurement in centimetres in the participant’s Instrument. Height should be recorded to the nearest centimetre

Record your Technician ID code in the space provided in the participant’s instrument.

Measuring Weight

Equipment: Seca digital portable scale. The equipment should be checked and calibrated each day.

Preparing the patient: Ask the participant to remove their footwear (shoes, slippers,sandals, etc) and socks.

Taking the measurement

Ask the participant to step onto scale with one foot on each side of the scale.

Ask the participant to:

stand still

face forward

place arms on the side and

wait until asked to step off.

Record the weight in kilograms on the participant's instrument. Weight should be measured to the nearest 0.1 and rounding up if midway

Measuring Waist Circumference

Equipments: To take waist circumference measurements you will need a:

constant tension tape (for example, Figure Finder Tape Measure)

pen

chair or coat stand for participants to place their clothes.

Privacy; A private area is necessary for this measurement. This could be a separate room, or an area that has been screened off from other people

Preparing the participant:

Measurement should be taken over light clothing; thick or bulky clothing must be removed.

How to take the measurement:

This measurement should be taken:at the end of a normal expiration; with the arms relaxed at the sides; at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest (hip bone).

Follow the steps below to measure the waist circumference of a participant:

Standing to the side of the participant, locate the last palpable rib and the top of the hip bone. You may ask the participant to assist you in locating these points on their body.

Ask the participant to wrap the tension tape around themselves and then position the tape at the midpoint of the last palpable rib and the top of the hip bone, making sure to wrap the tape over the same spot on the opposite side.

Note: Check that the tape is horizontal across the back and front of the participant and as parallel with the floor as possible.

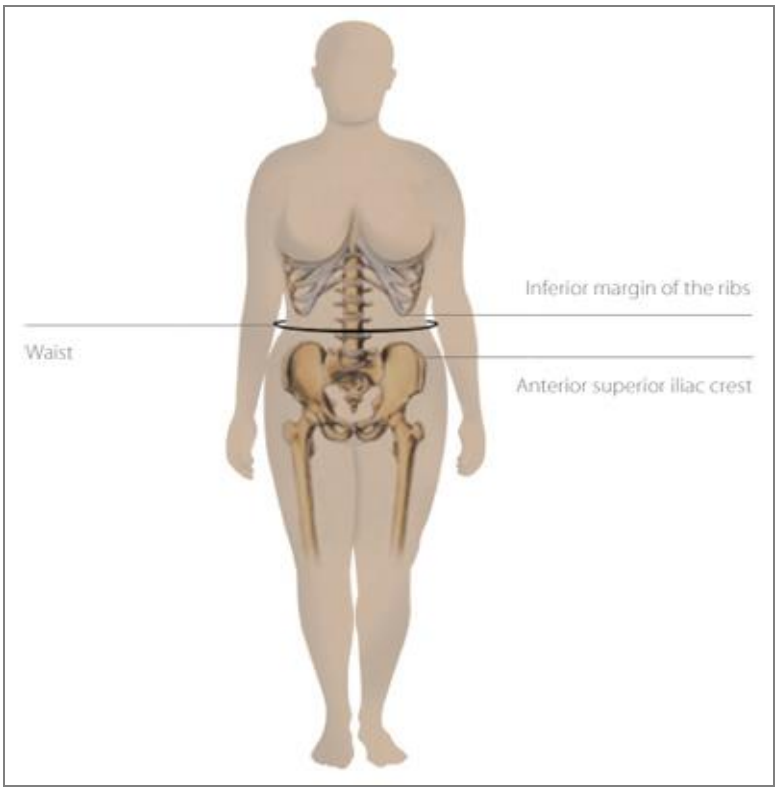
Ask the participant to:

stand with their feet together with weight evenly distributed across both feet;

hold the arms in a relaxed position at the sides;

breathe normally for a few breaths, then make a normal expiration.

Measure waist circumference and read the measurement at the level of the tape to the nearest 0.1 cm, making sure to keep the measuring tape snug but not tight enough to cause compression of the skin. Record the measurement on the participant's instrument.



Guide for Measuring WC adapted from diabetes atlas (2006)

Measuring Hip Circumference

Equipments needed; constant tension tape (for example, Figure Finder Tape Measure), pen, a chair or coat stand for participant's to place their clothes. Privacy; A private area is necessary for this measurement. Hip measurements are taken immediately after waist circumferences.

Preparing the participant

Ideally this measurement should be taken without clothing, that is, directly over the skin but for cultural reasons in this study the measurement will be taken over light clothing**.**

How to take the measurement

This measurement should be taken:

-with the arms relaxed at the sides

-at the maximum circumference over the buttocks

1. Stand to the side of the participant, and ask them to help wrap the tape around themselves
2. Position the measuring tape around the maximum circumference of the buttocks.
3. Ask the participant to:
    -stand with their feet together with weight evenly distributed over both feet;
    -hold their arms relaxed at the sides.
4. Check that the tape position is horizontal all around the body and snug without constricting.
5. Measure hip circumference and read the measurement at the level of the tape to the nearest 0.1 cm.
6. Record the measurement on the participant's instrument.

Note: Measure only once and record.

After completing the physical measurements direct the patient to the biochemical measurement station, where the patient will be given a morning appointment for fasting blood glucose measurement.

Biochemical Measurements

Fasting Blood Glucose

Equipment needed:

blood glucose measuring device (Hemoque 201)

test strips

lancet

cotton balls

sterile swabs

gloves

disposable container.

Preparing the patient

Patient should fast for at least 12 hours before the test. Ask the patient if they have been fasting for the past 12 hours. If the patient has not fasted correctly, explain to the patient the importance of fasting to the accuracy of the test and if they are willing give them another appointment to come back for the test.

Measuring blood glucose

Put on gloves

Remove a test strip

Rub and kneed a fingertip to help withdraw blood (rub the side of the participant's finger closest to the thumb)

Wipe or swab the fingertip by using a sterile swab

Lance the massaged place on the fingertip with lancing device.

Allow a hanging blood drop to form without applying too much pressure

Carefully apply the drop of blood to the test field on top of the strip without touching the test field directly to the finger.

Note: The test field must be completely covered with blood. If too little blood is applied, do not rub it in or apply a second drop, but repeat the measurement with a fresh test strip.

Give the participant a cotton ball to press on the puncture.

Put the test strip into the machine

Wait for the measurement to be displayed .The blood glucose results is usually displayed in mmol/L.

Record the results of the fasting blood sugar reading in the participant's instrument.

IMPORTANT SAFETY INFORMATION:
Sharps should be handled with care; you should not recap used syringes.
Dispose any sharps in the disposable container to avoid the risk of injuries.
Avoid direct contact with body fluids. Gloves must be worn when drawing blood. Does not re use gloves between patients
In case of blood spillage clean the surface immediately with JIK (sodium hypochlorite) solution; avoid direct skin contact with the disinfectant
In case of accidental injury with blood contaminated sharps, wash injured site immediately with soap and water, and report to the immediate supervisor
Report to the officer in charge of Post Exposure Prophylaxis (PEP) for evaluation and reporting
Label blood containers before putting in the sample
For more information on personal protection refer to the National infection prevention and control guidelines for health care services in Tanzania

Additional Tests

The additional tests include;

Biochemical measurements; Lipid profile, Renal function tests, Urinalysis and HbA1c

Electrocardiogram (ECG)

Biochemical measurements

The blood for biochemical measurements should be taken at the same seating, as soon as one obtains the results of the fasting blood glucose so that the patient does not have to fast again for the blood lipids measurement. You should clean hands with alcohol gel or clean with water before and after the procedure

Note: Experienced laboratory technician will be sought to do the venepunctures and handle the specimens.

Blood samples

Preparing the patient

The patient should be seated for the procedure and should be informed of the purpose for collecting the blood samples

Equipments needed;

Tourniquet

Cotton balls

Alcohol swabs,

Disposable container

Syringes

Appropriate blood containers

Procedure for taking blood samples

Place a tourniquet around the upper part of the patients arm, and pull fairly tight

Locate the vein in the anterior cubital fossae

Wipe the area with an antiseptic wipe and wait for this to dry

Insert a needle through the skin to the vein

On successful venous entry release the tourniquet

Extract blood via either a syringe with a needle, or vacuum tubes

Collect a total of about 5mls of blood into the different tubes as shown below

Remove the needle , apply a cotton swab and instruct the patient to apply pressure for one or two minutes

Make sure the blood samples are labelled correctly and placed on the rack at the bleeding station

The blood samples should then be sent to the laboratory.

Test	**Amount of blood**	**Collection tube**
Lipid profile and Renal Function tests	3mls	Plain
HbA1c	2mls	EDTA

IMPORTANT SAFETY INFORMATION:
Sharps should be handled with care; you should not recap used syringes.
Dispose any sharps in the disposable container to avoid the risk of injuries.
Avoid direct contact with body fluids. Gloves must be worn when drawing blood. Does not re use gloves between patients
In case of blood spillage clean the surface immediately with JIK (sodium hypochlorite) solution; avoid direct skin contact with the disinfectant
In case of accidental injury with blood contaminated sharps, wash injured site immediately with soap and water, and report to the immediate supervisor
Report to the officer in charge of Post Exposure Prophylaxis (PEP) for evaluation and reporting
Label blood containers before putting in the sample
For more information on personal protection refer to the National infection prevention and control guidelines for health care services in Tanzania

Collection of urine sample

Participants should also be given a labelled urine collection jar with a paper bag and asked to bring a morning sample of urine when they come back for the fasting blood glucose measurements. The samples should then be sent to the lab after receipt.

Participants should be explained the procedure for collecting the urine (mid stream urine Sample)

Assessment of Cardiovascular Complications

ECG Testing[2,3]

Equipments needed

Liquid gel

Cotton wool

Examination bed

Sticker labels

ECG machine

[2] ECG made easy

[3] ***Model protocol for diabetes and other NCDs by Dowse and Zimmet (1992)***

Preparing the patient

The patient should lie relaxed on the examination bed/couch. Ensure adequate privacy.

Explain the procedure to the patient and explain the reason for test.

Procedure for ECG testing

Ask the patient lies flat on a bed or table

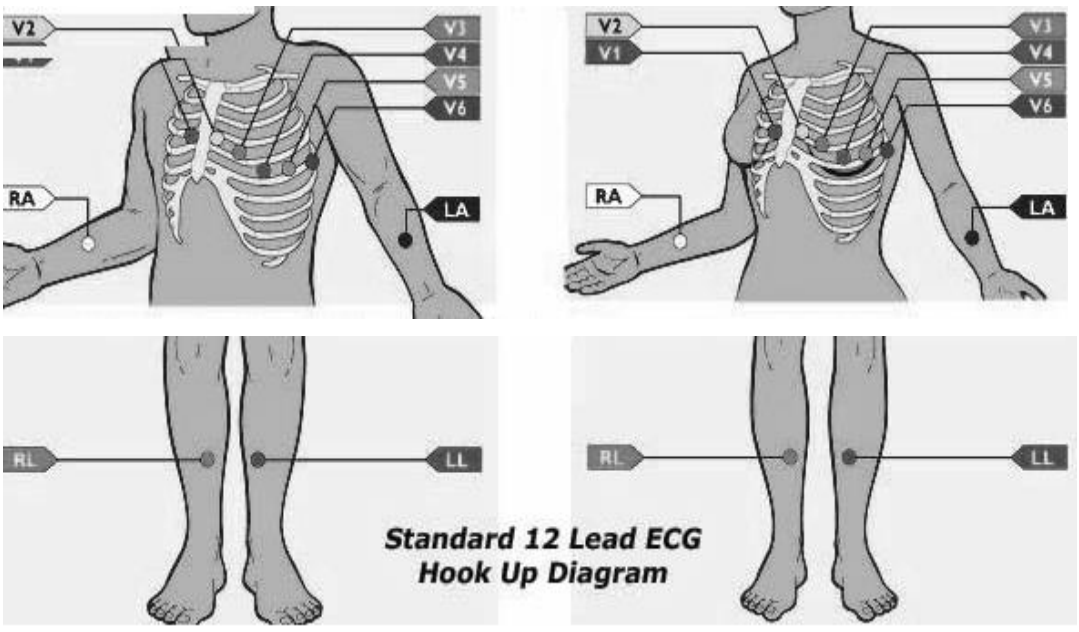
Apply a small amount of gel to the skin where the electrodes are to be applied

Attached to each extremity (four total) and to six pre-defined positions on the front of the chest (see fig below) Ask the patient to remain still throughout the test

Take the ECG recording

Place a sticker label containing patient's name and study number on the ECG tracing

Note: Position the chest electrodes as described below;
Lead **V1** - right sternal border, fourth intercostal space
Lead **V2** - left side of the sternum, fourth intercostal space
Lead **V3** - midway between leads V2 and V4
Lead **V4**- mid-clavicular line in the fifth intercostal space
Lead **V5** - anterior axillary line in the fifth intercostal space
Lead **V6** is at the mid-axillary line, fifth intercostal space



Positioning electrodes for the 12 lead ECG (Image adapted from davismedicalequipments.com)

Appendix 7 Study Questionnaires (English and Swahili versions)

Development and Validation of a Risk Score Tool for Diabetes in Tanzania and other African Populations

Diabetes Survey Questionnaire

2011

Investigator: **Mary Mayige**

Supervisors: **Dr Eugene Sobngwi**

Prof Richard Walker

Dr Richard Mcnally

General Information			
Location and Date		**Response**	**Code**
1	Centre ID		G1
2	Interviewer ID	⌊_⌊_⌊_⌋	G2
3	Date of completion of the interview	⌊_⌊_⌋ ⌊_⌊_⌋ ⌊_⌊_⌊_⌊_⌋ dd mm year	G3
	Participant Id Number	⌊_⌊_⌊_⌋ ⌊_⌊_⌊_⌋ ⌊_⌊_⌊_⌋	
Consent and Name		**Response**	**Code**
4	Consent has been read and obtained	Yes 1 No 2 **If NO, END**	G4
5	Time of starting interview (24 hour clock)	⌊_⌊_⌋ : ⌊_⌊_⌋ hrs mins	G5
6	Time of completing interview (24 hour clock)	⌊_⌊_⌋ : ⌊_⌊_⌋ hrs mins	G6
7	Time of interview (24 hour clock)	⌊_⌊_⌋ : ⌊_⌊_⌋ hrs mins	G7
8	Family Surname		G8
9	First Name		G9
Additional Information			
10	Contact phone number where possible		G10
11	Mention, Whose phone is it (circle the correct answer)	Office phone 1 Home 2 Neighbours' 3 Other 4	G11
		Other(please specify) ⌊_⌊_⌊_⌊_⌊_⌊_⌋	G11 other

Demographic Information			
Question		**Response**	**Code**
12	Sex (Record Male / Female as observed)	Male 1	DE1
		Female 2	
13	What is your date of birth?	⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ dd mm year Don't Know	DE2
14	How old are you?	Years ⌊_⌋⌊_⌋	DE3
15	What is the highest level of education you have completed?	No formal schooling 1	DE4
		Less than primary school 2	
		Primary school completed 3	
		Secondary school completed 4	
		High school completed 5	
		College/University completed 6	
		Post graduate degree 7	
		Refused 88	
16	What is your marital status?	Never married 1	DE5
		Currently married 2	
		Separated 3	
		Divorced 4	
		Widowed 5	
		Cohabitating 6	
		Refused 88	
17	Which of the following best describes your main work status over the past 12 months?	Government employee 1	DE6
		Non-government employee 2	
		Self-employed 3	
		Non-paid 4	
		Student 5	
		Homemaker 6	
		Retired 7	
		Unemployed (able to work) 8	
		Unemployed (unable to work) 9	
		Refused 88	
18	Taking the past year, can you tell me what the average earnings of the household have been? (RECORD ONLY ONE, NOT ALL 3)	Per week ⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ Go to T1	DE7a
		OR per month ⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ Go to T1	DE7b
		OR per year ⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ Go to T1	DE7c
		Refused 88	DE7d
		More than 250,000, ≤ 500,000 2	DE7e
		More than 500,000, ≤ 750,000 3	

		More than 750,000, ≤ 1,000,000	4
		More than 1,000,000	5
		Don't Know	77

Behavioral Measurements

Tobacco Use

Now I am going to ask you some questions about various health behaviors. This includes things like smoking, drinking alcohol, eating fruits and vegetables and physical activity. Let's start with tobacco.

Question		**Response**		**Code**
20	Do you currently smoke any tobacco products, such as cigarettes, cigars or pipes? (USE SHOWCARD)	Yes	1	T1
		No	2 If No, go to T6	
21	Do you currently smoke tobacco products daily?	Yes	1	T2
		No	2 If No, go to T6	
22	How old were you when you first started smoking daily?	Age (years)		T3
		Don't know 77	⌊_⌋⌊_⌋ If Known, go to T5a	
23	Do you remember how long ago it was? (RECORD ONLY 1, NOT ALL 3) Don't know 77	In Years	⌊_⌋⌊_⌋ If Known, go to T5a	T4a
		OR in Months	⌊_⌋⌊_⌋ If Known, go to T5a	T4b
		OR in Weeks	⌊_⌋⌊_⌋	T4c
24	On average, how many of the following do you smoke each day? (RECORD FOR EACH TYPE, USE SHOWCARD) Don't Know 77	Manufactured cigarettes	⌊_⌋⌊_⌋	T5a
		Hand-rolled cigarettes	⌊_⌋⌊_⌋	T5b
		Pipes full of tobacco	⌊_⌋⌊_⌋	T5c
		Cigars, cheroots, cigarillos	⌊_⌋⌊_⌋	T5d
		Other	⌊_⌋⌊_⌋ If Other, go to T5other, else go to T9	T5e
		Other (please specify):	⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ Go to T9	T5other
25	In the past, did you ever smoke daily?	Yes	1	T6
		No	2 If No, go to T9	
26	How old were you when you stopped smoking daily?	Age (years)		T7
		Don't Know 77	⌊_⌋⌊_⌋ If Known, go to T9	
27	How long ago did you stop smoking daily? (RECORD ONLY 1, NOT ALL 3) Don't Know 77	Years ago	⌊_⌋⌊_⌋ If Known, go to T9	T8a
		OR Months ago	⌊_⌋⌊_⌋ If Known, go to T9	T8b
		OR Weeks ago	⌊_⌋⌊_⌋	T8c
28	Do you currently use any smokeless tobacco such as [snuff, chewing tobacco, betel]? (USE SHOWCARD)	Yes	1	T9
		No	2 If No, go to T12	

29	Do you currently use smokeless tobacco products daily?	Yes	1	T10
		No	2 If No, go to T12	
30	In the past, did you ever use smokeless tobacco such as [snuff, chewing tobacco, or betel] daily?	Yes	1	T11
		No	2	
31	During the past 7 days, on how many days did someone in your home smoke when you were present?	Number of days		T12
		Don't know 77	⌊_⌋⌊_⌋	
32	During the past 7 days, on how many days did someone smoke in closed areas in your workplace (in the building, in a work area or a specific office) when you were present?	Number of days		T13
		Don't know or don't work in a closed area 77	⌊_⌋⌊_⌋	
Alcohol Consumption				
The next questions ask about the consumption of alcohol.				
33	Have you ever consumed an alcoholic drink such as beer, wine, spirits, fermented cider or local brew? (USE SHOWCARD OR SHOW EXAMPLES)	Yes	1	A1a
		No	2 If No, go to D1	
34	Have you consumed an alcoholic drink within the past 12 months?	Yes	1	A1b
		No	2 If No, go to D1	
35	During the past 12 months, how frequently have you had at least one alcoholic drink? (READ RESPONSES, USE SHOWCARD)	Daily	1	A2
		5-6 days per week	2	
		1-4 days per week	3	
		1-3 days per month	4	
		Less than once a month	5	
36	Have you consumed an alcoholic drink within the past 30 days?	Yes	1	A3
		No	2 If No, go to D1	
37	During the past 30 days, on how many occasions did you have at least one alcoholic drink?	Number Don't know 77	⌊_⌋⌊_⌋	A4
38	During the past 30 days, when you drank alcohol, on average, how many standard alcoholic drinks did you have during one drinking occasion? (USE SHOWCARD)	Number Don't know 77	⌊_⌋⌊_⌋	A5
39	During the past 30 days, what was the largest number of standard alcoholic drinks you had on a single occasion, counting all types of alcoholic drinks together?	Largest number Don't Know 77	⌊_⌋⌊_⌋	A6
41	During each of the past 7 days, how many standard alcoholic drinks did you have each day? (USE SHOWCARD) Don't Know 77	Monday	⌊_⌋⌊_⌋	A8a
		Tuesday	⌊_⌋⌊_⌋	A8b
		Wednesday	⌊_⌋⌊_⌋	A8c
		Thursday	⌊_⌋⌊_⌋	A8d

		Friday ⌊_⌋⌊_⌋	A8e
		Saturday ⌊_⌋⌊_⌋	A8f
		Sunday ⌊_⌋⌊_⌋	A8g

Diet

The next questions ask about the fruits and vegetables that you usually eat. I have a nutrition card here that shows you some examples of local fruits and vegetables. Each picture represents the size of a serving. As you answer these questions please think of a typical week in the last year.

	Question	**Response**	**Code**
42	In a typical week, on how many days do you eat fruit? *(USE SHOWCARD)*	Number of days ⌊_⌋⌊_⌋ Don't Know 77 If Zero days, go to D3	*D1*
43	How many servings of fruit do you eat on one of those days? (*USE SHOWCARD)*	Number of servings ⌊_⌋⌊_⌋ Don't Know 77	*D2*
44	In a typical week, on how many days do you eat vegetables? *(USE SHOWCARD)*	Number of days ⌊_⌋⌊_⌋ Don't Know 77 If Zero days, go to D5	D3
45	How many servings of vegetables do you eat on one of those days? *(USE SHOWCARD)*	Number of servings ⌊_⌋⌊_⌋ Don't know 77	D4
46	On average, how many meals per week do you eat that were not prepared at a home? By meal, I mean breakfast, lunch and dinner.	Number ⌊_⌋⌊_⌋ Don't know 77	D5

Physical Activity

Next I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person.
Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

	Question	**Response**	**Code**
Work			
47	Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like lifting heavy loads, manual construction work, digging etc for at least 10 minutes continuously? *(USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 4*	*P1*
48	In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	Number of days ⌊_⌋	*P2*
49	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours : minutes ⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ hrs mins	P3 (a-b)
50	Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate	Yes 1	P4

	such as brisk walking, *carrying light loads, doing chores like cleaning, washing or ironing clothes etc* ,for at least 10 minutes continuously?	No 2 *If No, go to P 7*	
51	In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days ⌊__⌋	P5
52	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P6 (a-b)
Travel to and from places			
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship.			
53	Do you walk or use a bicycle *(pedal cycle)* for at least 10 minutes continuously to get to and from places?	Yes 1	P7
		No 2 *If No, go to P 10*	
54	In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	Number of days ⌊__⌋	P8
55	How much time do you spend walking or bicycling for travel on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P9 (a-b)
Recreational activities			
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure)			
56	Do you do any vigorous-intensity sports, fitness or recreational *(leisure)* activities that cause large increases in breathing or heart rate like *running, playing football etc*, for at least 10 minutes continuously? *(USE SHOWCARD)*	Yes 1	P10
		No 2 *If No, go to P 13*	
57	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational *(leisure)* activities?	Number of days ⌊__⌋	P11
58	How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P12 (a-b)
59	Do you do any moderate-intensity sports, fitness or recreational *(leisure)* activities that cause a small increase in breathing or heart rate such as brisk walking, *cycling, swimming, dancing* etc for at least 10 minutes continuously? *(USE SHOWCARD)*	Yes 1	P13
		No 2 *If No, go to P16*	
60	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational *(leisure)* activities?	Number of days ⌊__⌋	P14
61	How much time do you spend doing moderate-intensity sports, fitness or recreational *(leisure)* activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋	P15 (a-b)

Sedentary behavior			
The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, traveling in car, bus, train, reading, playing cards or watching television, but do not include time spent sleeping. *(USE SHOWCARD)*			
62	How much time do you usually spend sitting or reclining on a typical day?	Hours : minutes ⌊_⌊_⌋ : ⌊_⌊_⌋	P16 (a-b)

Personal History			
History of Raised Blood Pressure			
Question		**Response**	**Code**
63	Have you ever had your blood pressure measured by a doctor or other health worker?	Yes 1 No 2 *If No, go to H6*	H1
64	Have you ever been told by a doctor or other health worker that you have raised blood pressure or hypertension?	Yes 1 No 2 *If No, go to H6*	H2a
65	Have you been told in the past 12 months?	Yes 1 No 2	H2b
66	*Are you currently receiving any of the following treatments/advice for high blood pressure prescribed by a doctor or other health worker?*		
	Drugs (medication) that you have taken in the past two weeks	Yes 1 No 2	H3a
	Advice to reduce salt intake	Yes 1 No 2	H3b
	Advice or treatment to lose weight	Yes 1 No 2	H3c
	Advice or treatment to stop smoking	Yes 1 No 2	H3d
	Advice to start or do more exercise	Yes 1 No 2	H3e
67	Have you ever seen a traditional healer for raised blood pressure or hypertension?	Yes 1 No 2	H4

68	Are you currently taking any herbal or traditional remedy for your raised blood pressure?	Yes No	1 2	H5
History of Raised Blood Sugar				
Question		**Response**		**Code**
69	Have you ever had your blood sugar measured by a doctor or other health worker?	Yes No	1 2 *If No, go to H8*	H6
70	Have you ever been told by a doctor or other health worker that you have raised blood sugar?	Yes No	1 2 *If No, go to H8*	H7a
71	Have you been told in the past 12 months?	Yes No	1 2	H7b
Other past Illnesses				
72	Previous history of stroke	Yes No Don't Know	1 2 777	H8
73	Previous history of heart disease	Yes No Don't Know	1 2 777	H9
Family History of Cardiovascular Diseases (Do you have any first degree relative mother, father, child, sister or brother with any of the following)				
74	Hypertension	Yes No Don't Know	1 2 777	H10
75	Diabetes	Yes No Don't Know	1 2 777	H11
76	Stroke	Yes No Don't Know	1 2 777	H12
77	Heart Disease	Yes No Don't Know	1 2 777	H13

Physical Measurements			
Height and Weight			
Question		**Response**	**Code**
78	Interviewer ID	⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M1
79	Device IDs for height and weight	Height ⌊_⌋⌊_⌋	M2a
		Weight ⌊_⌋⌊_⌋	M2b
80	Height	cm ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ . ⌊_⌋	M3
81	Weight *If too large for scale 666.6*	kg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ . ⌊_⌋	M4
82	For women: Are you pregnant?	Yes 1 *If Yes, go to M 8*	M5
		No 2	
Waist and Hip			
83	Device ID for waist	⌊_⌋⌊_⌋⌊_⌋	M6
84	Waist circumference	cm ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ . ⌊_⌋	M7
85	Hip circumference	cm ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ . ⌊_⌋	M8
Blood Pressure			
86	Interviewer ID	⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M9
87	Device ID for blood pressure	⌊_⌋⌊_⌋⌊_⌋	M10
88	Cuff size used	Small 1	M11
		Medium 2	
		Large 3	
89	Reading 1	SBP mmHg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M12a
		DBP mmHg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M12b
90	Reading 2	SBP mmHg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M13a
		DBP mmHg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M13b
91	Reading 3	SBP mmHg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M14a
		DBP mmHg ⌊_⌋⌊_⌋⌊_⌋⌊_⌋	M14b
92	During the past two weeks, have you been treated for raised blood pressure with drugs (medication) prescribed by a doctor or other health worker?	Yes 1	M15
		No 2	
93	Heart Rate		
	Reading 1	Beats/min ⌊_⌋⌊_⌋⌊_⌋	M16a

	Reading 2	Beats/min ⌊_⌋⌊_⌋⌊_⌋	M16b
	Reading 3	Beats /min ⌊_⌋⌊_⌋⌊_⌋	M16c

Biochemical Measurements

Blood Glucose

	Question	**Response**	**Code**
94	During the past 12 hours have you had anything to eat or drink, other than water?	Yes 1 No 2	B1
95	Technician ID	⌊_⌋⌊_⌋⌊_⌋	B2
96	Device ID	⌊_⌋⌊_⌋	B3
97	Fasting blood glucose: *mmol/l*	mmol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B4

Additional measurements for Participants

Blood Lipids

98	During the past two weeks, have you been treated for raised cholesterol with drugs (medication) prescribed by a doctor or other health worker?	Yes 1 No 2	B5
99	HDL Cholesterol	mmol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B6
100	LDL Cholesterol	mmol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B7
101	Triglycerides *mmol/l*	mmol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B8
102	Total cholesterol*: mmol/l*	mmol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B9
Renal Function Tests and Urinary Albumin excretion			
103	Serum Creatinine	umol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B10
104	Urine Albumin	mg/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B11
105	Urine Creatinine	umol/l ⌊_⌋⌊_⌋.⌊_⌋⌊_⌋	B12

Development and Validation of a Risk Score Tool for Diabetes in Tanzania and other African Populations

Diabetes Survey Questionnaire (Swahili Version)

2011

Investigator: **Mary Mayige**

Supervisors: **Dr Eugene Sobngwi**

Prof Richard Walker

Dr Richard Mcnally

Dr Richard Mcnally

Taarifa za awali			
Mahali na Tarehe		**Jibu**	**Code**
1	Alama ya kituo	⌊_⌋⌊_⌋	G1
2	Utambulisho wa Mhojaji	⌊_⌋⌊_⌋⌊_⌋	G2
3	Tarehe ya kukamilisha dodoso	⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ tarehe mwezi mwaka	G3
Namba ya Mhojiwa ⌊_⌋⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋⌊_⌋			
Ridhaa, Lugha ya mahojiano na Jina la Mhojiwa			
Jibu			**Code**
4	Mhojiwa amesomewa fomu ya Ridhaa na ridhaa imepatikana	Ndio 1 Hapana 2 **Kama Hapana, MWISHO**	G4
		Hapana 2 **Kama Hapana, MWISHO**	
5	Muda wa kuanza mahojiano	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ masaa dakika	G5
6	Muda wa kumaliza mahojiano	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ Masaa dakika	G6
7	Muda wa mahojiano (masaa 24)	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ masaa dakika	G7
8	Jina la ukoo/ mwisho la mhojiwa		G8
9	Jina la kwanza la mhojiwa		G9
Maelezo ya ziada			
10	Namba ya simu ya mhojiwa inapowezekana		G10
11	Taja simu ni ya nani	Kazini 1 Nyumbani 2 Jirani 3 Nyingine (elezea) 4	G11
		Nyingine ⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋	G11 other

Maelezo ya demografia				
Maswali		**Jibu**		**Code**
12	Jinsi (*Andika Mume/Mke kama inavyoonekana)*	Mume	1	DE1
		Mke	2	
13	Tarehe yako ya kuzaliwa ni ipi? *Sijui 77 777 7777*	⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋⌊_⌋⌊_⌋ tarehe mwezi mwaka	*Kama inafahamika, nenda C4*	DE2
14	Una miaka mingapi?	Miaka	⌊_⌋⌊_⌋	DE3
15	Ni kiwango gani cha elimu cha juu zaidi ulichofikia?	Sijasoma	1	DE4
		Sikumaliza elimu ya msingi	2	
		Nimemaliza elimu ya msingi	3	
		Nimemaliza elimu ya	4	
		Nimemaliza elimu ya juu ya	5	
		Nimemaliza Chuo/Chuo Kikuu	6	
		Elimu baada ya shahada ya kwanza(uzamili/uzamivu)	7	
		Amekataa kujibu	88	
16	Hali ya Ndoa	Sijawahi kuoa/ kuolewa	1	DE5
		Nimeoa/ nimeolewa	2	
		Tumetengana	3	
		Mtalaka	4	
		Mjane	5	
		Tunaishi pamoja bila ndoa	6	
		Amekataa kujibu	88	
17	Ni ipi kati ya haya yafuatayo yanaelezea vizuri kazi ambayo umekuwa ukifanya katika miezi 12 iliyopita?	Mtumishi wa Serikali	1	DE6
		Mtumishi asiye wa Serikali	2	
		Nimejiajiri mwenyewe	3	
		Kazi/shughuli bila malipo	4	
		Mwanafunzi	5	
		Shughuli za nyumbani	6	
		Mstaafu	7	
		Sina kazi (ana uwezo wa kufanya kazi)	8	
		Sina kazi (hana uwezo wa kufanya kazi)	9	
		Amekataa kujibu	88	
18	Katika mwaka mmoja uliopita, naomba unitajie wastani wa mapato ya kaya yako ni kiasi gani? *(JIBU MOJA TU)*	Kwa juma	⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ *Nanda swali T1*	DE7a
		AU Kwa mwezi	⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ *Nenda swali T1*	DE7b
		AU Kwa mwaka	⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋ *Nenda swali T1*	DE7c
		Amekataa kujibu	88	DE7d

19	Ikiwa hufahamu ni kiasi gani , unaweza kutoa **makisio/makadirio** ya jumla ya mapato ya kaya yako kwa mwaka (kwa shilingi za kitanzania) ikiwa nitakusomea majibu yafuatayo? Je ni, *(MSOMEE MAJIBU YOTE)*	≤ 250,000 1 Zaidi ya 250,000 ≤ 500,000 2 Zaidi ya 500,000 ≤ 750,000 3 Zaidi ya 750,000 ≤ 1,000,000 4 Zaidi ya 1,000,000 5 Sifahamu 7 Amekataa kujibu 88	DE8

Kipimo cha mwenendo wa tabia

Utumiaji wa Tumbaku

Sasa nitakuuliza maswali yanayohusiana na tabia/mazoea mbalimbali yanayohusu afya. Haya yanahusisha masuala ya uvutaji sigara/tumbaku, unywaji wa pombe, ulaji wa matunda ma mbogamboga na mazoezi ya mwili. Tuanze na sigara/tumbaku.

Maswali		**Jibu**	**Code**
20	Je, kwa sasa unavuta aina yoyote ya tumbaku kama vile sigara, kiko, sigara ya kusokota n.k?	Ndio 1 Hapana 2 *Kama Hapana, nenda T6*	T1
21	**<u>Kama Ndio,</u>** Kwa sasa unavuta sigara au tumbaku **kila siku**?	Ndio 1 Hapana 2 *Kama Hapana, nenda T6*	T2
22	Ulikuwa na umri gani ulipoanza kuvuta sigara kila siku **kwa mara ya kwanza**?	Umri (miaka) ⌊_⌋⌊_⌋ *Kama inafahamika, nenda T5a* Sikumbuki 777	T3
23	Unakumbuka ni muda gani uliopita? *(JIBU MOJA TU)* Sikumbuki 77	Kwa miaka ⌊_⌋⌊_⌋ *Kama inafahamika, nenda T5a*	T4a
		AU kwa miezi ⌊_⌋⌊_⌋ *Kama inafahamika, nenda T5a*	T4b
		AU kwa majuma ⌊_⌋⌊_⌋	T4c
24	Kwa wastani, unavuta **kiasi gani** kwa siku cha kila moja ya aina zifuatazo za tumbaku?	Sigara zinazotengenezwa viwandani ⌊_⌋⌊_⌋	T5a
		Sigara /tumbaku za kusokota kwa mikono ⌊_⌋⌊_⌋	T5b
	(JAZA KWA KILA MOJA)	Kiko kilichojazwa tumbaku/sigara ⌊_⌋⌊_⌋	T5c
	Sikumbuki 77	Biri(Cigars) ⌊_⌋⌊_⌋	T5d
		Aina nyingine ⌊_⌋⌊_⌋ *Kama aina nyingine, nenda T5 other*	T5e
		Aina nyingine (zitaje tafadhali): ⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋⌊_⌋	T5 other
25	Hapo zamani, **ulishawahi** kuvuta sigara/tumbaku **kila siku**?	Ndio 1 Hapana 2 *Kama Hapana, nenda T9*	T6
26	**<u>Kama Ndio</u>**, ulikuwa na miaka mingapi **ulipoacha** kuvuta sigara/tumbaku **kila siku**?	Umri (miaka) ⌊_⌋⌊_⌋ *Kama inafahamika, nenda T9* Sikumbuki 77	T7

27	**Ni muda gani umepita** tangu ulipoacha kuvuta sigara/tumbaku kila siku? *(JIBU MOJA TU)* Sikumbuki 77	Miaka	⌊_⌊_⌊_⌋ *Kama inafahamika, nenda T9*	T8a
		AU Miezi	⌊_⌊_⌋ *Kama inafahamika, nenda T9*	T8b
		AU Majuma	⌊_⌊_⌋	T8c
28	**Kwa sasa** unatumia aina yoyote ya tumbaku **isiyo ya kuvuta** kama vile ugoro, 'kuber' n.k.?	Ndio	1	T9
		Hapana	2 *Kama Hapana, nenda T12*	
29	**Kwa sasa, unatumia tumbaku isiyo ya kuvuta kila siku?**	Ndio	1	T10
		Hapana	2 *Kama Hapana, nenda T12*	
30	Hapo zamani, **ulishawahi** kutumia aina yoyote ya tumbaku isiyo ya kuvuta kama vile ugoro, 'kuber' n.k. **kila siku**?	Ndio	1	T11
		Hapana	2	
31	Ndani ya siku saba zilizopita, ni siku ngapi mtu mnayeishi naye ndani ya nyumba amevuta sigara ukiwepo?	Siku	⌊_⌊_⌋ Sijui 77	T12
32	Ndani ya siku saba zilizopita, ni siku ngapi mtu amevuta sigara kwenye eneo lisilo la wazi kazini ukiwepo?	Siku	⌊_⌊_⌋ Sijui au nafanya kazi kwenye eneo la wazi 77	T13

Utumiaji wa Pombe/Vileo

Maswali yafuatayo yanauliza kuhusu utumiaji wa pombe/Vileo

Maswali		**Jibu**		**Code**
33	Je, umewahi kutumia kinywaji chenye kilevi (kama vile bia, mvinyo, pombe kali au pombe ya kienyeji) katika **miezi 12 iliyopita**? *(TUMIA kadi ya kielelezo AU TOA MIFANO)*	Ndio	1	A1a
		Hapana	2 *Kama Hapana, nenda D1*	
34	Je umekunywa kinywaji chenye kilevi ndani ya miezi 12 iliyopita?	Ndio	1	A1b
		Hapana	2 *Kama Hapana, nenda D1*	
35	Katika miezi 12 iliyopita, **ni mara ngapi** umekunywa angalau kinywaji kimoja chenye kilevi? *(MSOMEE MAJIBU, TUMIA kadi ya kielelezo)*	Kila siku	1	A2
		Siku 5-6 kwa juma	2	
		Siku 1-4 kwa juma	3	
		Siku 1-3 kwa mwezi	4	
		Chini ya mara 1 kwa mwezi	5	
36	Umetumia kinywaji chenye kilevi (kama vile bia, mvinyo, pombe kali au pombe ya kienyeji) katika **siku 30 zilizopita**? *(TUMIA kadi ya kielelezo AU TOA MIFANO)*	Ndio	1	A3
		Hapana	2 *Kama Hapana, nenda D1*	
37	Katika **siku 30** zilizopita, **ni mara ngapi** umekunywa angalau kinywaji kimoja chenye kilevi?	Mara	⌊_⌊_⌋ Sijui 77	A4
38	Katika siku 30 zilizopita, ulipokunywa kinywaji chenye kilevi, kwa makisio ulikunywa vinywaji vingapi (standard drinks) kwa mkupuo (*TUMIA KADI YA KIELELEZO)*	Mara	⌊_⌊_⌋ Sijui 77	A5
39	Katika siku 30 zilizopita , ulipokunywa kinywaji	Idadi kubwa zaidi ya	⌊_⌊_⌋	A6

	chenye kilevi , ni kiasi gani **kikubwa** ulichokunywa (standard drink) siku uliyokunywa zaidi kwenye mkupuo mmoja ukijumlisha vinywaji vyote?	vinywaji Sijui 77	
40	Katika siku 30 zilizopita, ni mara ngapi umekunywa Kinywaji chenye kilevi (standard drink); **Kwa wanaume**: 5 au zaidi **Kwa wanawake**: 4 au zaidi ; kwenye mkupuo mmoja?	Mara ⌊_⌊_⌋ Sijui 77	A7
41	Katika **siku 7 zilizopita**, umekunywa vinywaji vingapi (standard drinks) vyenye kilevi katika kila siku ya wiki? *(JAZA KWA KILA SIKU, TUMIA kadi ya kielelezo)* Sifahamu 77	Jumatatu ⌊_⌊_⌋ Jumanne ⌊_⌊_⌋ Jumatano ⌊_⌊_⌋ Alhamisi ⌊_⌊_⌋ Ijumaa ⌊_⌊_⌋ Jumamosi ⌊_⌊_⌋ Jumapili ⌊_⌊_⌋	A8a A8b A8c A8d A8e A8f A8g

Lishe

Maswali yafuatayo yanauliza kuhusu matunda na mbogamboga ambazo unakula mara kwa mara. Hapa nina kadi ya maelezo ya lishe yenye mifano ya matunda na mbogamboga zinazopatikana katika maeneo yako. Kila picha inawakilisha kipimo kimoja. Unapojibu maswali haya tafadhali fikiria wiki moja ya kawaida katika mwaka uliopita.

Maswali		**Jibu**	**Code**
42	Kwa kawaida ni siku ngapi ndani ya wiki moja unakula **matunda**? *(TUMIA SHOWCARD*)	Idadi ya siku ⌊_⌊_⌋ Sifahamu 77 Kama siku 0, nenda D3	*D1*
43	Unakula matunda kipimo gani katika moja ya siku hizo? *(TUMIA SHOWCARD)*	Idadi ya vipimo ⌊_⌊_⌋ Sifahamu 77	D2
44	Kwa kawaida ni siku ngapi ndani ya wiki moja unakula **mbogamboga**? *(TUMIA SHOWCARD*)	Idadi ya siku ⌊_⌊_⌋ Sifahamu 77 *Kama siku 0, nenda D5*	D3
45	Unakula mbogamboga kipimo gani katika moja ya siku hizo? *(TUMIA SHOWCARD)*	Idadi ya Vipimo ⌊_⌊_⌋ Sifahamu 77	D4
46	Kwa wastani huwa unakula milo mingapi kwa wiki ambayo haijaandaliwa nyumbani? Mlo hapa ni kifungua kinywa, mlo wa mchana na ule wa jioni	Idadi ya milo ⌊_⌊_⌋ Sifahamu 77	D5

Mazoezi ya viungo

Sasa nitaendelea kukuuliza kuhusu muda unaotumia kufanya shughuli mbalimbali zinazohusu mazoezi ya viungo katika wiki moja ya kawaida. Tafadhali ujibu maswali haya hata kama unadhani wewe si mtu wa kufanya mazoezi mara kwa mara.
Kwanza tafakari kuhusu muda unaotumia kufanya kazi. Tunaposema kazi tunamaanisha shughuli zozote unazofanya zikiwemo zinazokuingizia kipato na zisizokuingizia kipato, mfano kuvua samaki, masomo, shughuli za nyumbani, kilimo, kuvuna mazao, kutafuta kazi n.k. Katika kujibu maswali haya 'shughuli za kutumia nguvu – kasi sana ni shughuli ambazo zinahitaji nguvu nyingi na husababisha ongezeko kubwa katika kupumua au mapigo ya moyo, shughuli za kutumia nguvu-kasi kiasi ' ni shughuli zinazohitaji nguvu ya kiasi na husababisha ongezeko dogo katika kupumua na mapigo ya moyo

Maswali		**Jibu**	**Code**
Mazoezi wakati wa kazi			
47	Je, kazi yako inahusisha shughuli za kutumia nguvu ambazo zinaongeza kasi ya kupumua na mapigo ya moyo kama vile kubeba mizigo mizito, kumwaga zege, kupiga kokoto, kuchota maji, kusomba mazao, kilimo au kazi za ujenzi kwa angalau dakika 10 mfululizo? *(TUMIA SHOWCARD)*	Ndio 1 Hapana 2 *Kama Hapana, nenda P 4*	P1
48	Katika wiki ya kawaida, ni kwa siku ngapi unafanya shughuli hizo za kutumia nguvu nyingi	Idadi ya siku ⌊_⌋	P2

	katika kazi yako?		
49	Unatumia muda gani kufanya shughuli za nguvu katika siku moja ya kazi?	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ Masaa Dakika	P3
50	Kazi yako inahusisha shughuli za kutumia nguvu kiasi ambazo zinaongeza kidogo kasi ya kupumua na mapigo ya moyo kama vile kutembea kwa haraka, kubeba mizigo isiyo mizito, kudeki, kufagia, kuosha vyombo, kufua, kupika, kupiga pasi, kuvuna mazao kwa angalau dakika 10 mfululizo? *(TUMIA SHOWCARD)*	Ndio 1	
		Hapana 2 *Kama Hapana, nenda P 7*	P4
51	Katika wiki ya kawaida, ni kwa siku ngapi unafanya shughuli hizo za kutumia nguvu kiasi katika kazi yako?	Idadi ya siku ⌊_⌋	P5
52	Unatumia muda gani kufanya shughuli za nguvu kiasi katika siku moja ya kazi?	⌊_⌋⌊_⌋ ⌊_⌋⌊_⌋ Masaa : dakika	P6 (a-b
Safari ya kwenda na kurudi toke sehemu moja hadi nyingine			
Maswali yafuatayo hayahusishi shughuli unazofanya wakati wa kazi ambazo umeshazitaja. Sasa ningependa kukuuliza kuhusu aina ya usafiri unaotumia kwenda sehemu mbalimbali kama vile sokoni, shambani, kanisani, msikitini n.k.			
53	Una kawaida ya kutembea kwa miguu au kwa kutumia baiskeli kwa angalau dakika 10 mfululizo wakati unapokwenda mahali fulani?	Ndio 1	P7
		Hapana 2 *Kama Hapana, nenda P 10*	
54	Katika wiki ya kawaida, unatumia siku ngapi kutembea kwa miguu au kwa kutumia baiskeli kwa angalau dakika 10 mfululizo wakati unapokwenda mahali fulani?	Idadi ya siku ⌊_⌋	P8
55	Unatumia muda gani kutembea kwa miguu au kwa kutumia baiskeli katika siku moja ya kawaida?	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ Masaa : dakika	P9
Mazoezi wakati wa mapumziko			
Sasa nitakuuliza maswali yahusuyo shughuli mbalimbali unazofanya wakati wako wa mapumziko, kwa mfano mazoezi ya viungo, michezo mbalimbali n.k. Usijumuishe shughuli unazofanya wakati wa kazi au kusafiri ambazo umeshajitaja hapo awali.			
56	Una kawaida ya kushiriki katika shughuli za michezo au mazoezi ambazo zinaongeza kwa kiasi kikubwa kasi ya kupumua au mapigo ya moyo kama vile kukimbia, kuruka kichura, kuinama na kuinuka, kuruka viunzi, kucheza nmpira kwa angalau dakika 10 mfululizo? *(TUMIA SHOWCARD)*	Ndio 1	P 10
		Hapana 2 *Kama Hapana, nenda P13*	
57	Katika wiki ya kawaida, unatumia siku ngapi kufanya shughuli hizo za michezo au mazoezi?	Idadi ya siku ⌊_⌋	P 11
58	Katika siku ya kawaida, unatumia muda gani kufanya shughuli hizo za michezo au mazoezi?	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ Masaa : dakika	P 12
59	Una kawaida ya kushiriki katika shughuli za michezo au mazoezi ambazo zinaongeza kwa kiasi kidogo kasi ya kupumua au mapigo ya moyo kama vile kuendesha, baiskeli, kutembea, kuogelea, kuimba kwa vitendo kwa angalau dakika 10 mfululizo? *(TUMIA SHOWCARD)*	1 Ndiyo 2 Hapana	
		Kama Hapana, nenda P16	P13

60	Katika wiki ya kawaida, unatumia siku ngapi kufanya shughuli hizo za michezo au mazoezi?	Idadi ya siku ⌊_⌋	P 14
61	Katika siku ya kawaida, unatumia muda gani kufanya shughuli hizo za michezo au mazoezi?	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ Masaa : dakika	P15

Tabia ya kukaa pasipo kujishughulisha

Swali lifuatalo linahusu muda uliotumia kukaa au kujinyoosha/kujiegemeza kujilaza wakati wa kazi, katika usafiri, kukaa na marafiki, kuangalia televisheni n.k. lakini bila kujumuisha muda uliotumia kulala. *(TUMIA SHOWCARD)*

62	Kwa kawaida unatumia muda gani kukaa au kujinyoosha kujilaza katika siku moja mfano ukiwa unaangalia TV, unasikiliza redio, unasoma gazeti au vitabu nk	?	⌊_⌋⌊_⌋ : ⌊_⌋⌊_⌋ Masaa : dakika	P16 (a-b)

Historia ya Mhojiwa

Historia ya Ongezeko la Shinikizo la Damu

Maswali		**Jibu**		**Code**
63	Je umeshawahi kupimwa na daktari au mtaalam wa afya?	Ndiyo Hapana	1 2 *kama hapana, nenda H6*	H1
64	Je umeshawahi kuambiwa na daktari au mtaalam wa afya kuwa una shinikizo la damu, au presha yako iko juu kuliko kawaida?	Ndiyo Hapana	1 2 *kama hapana, nenda H6*	H2a
65	Je umeambiwa hivyo ndani ya miezi 12 iliyopita?	Ndiyo Hapana	1 2	H2b
66	Kwa sasa unapata matibabu au ushauri kwa ajili ya ongezeko la shinikizo la damu kutoka kwa daktari au mtaalamu mwingine wa afya?			
	Dawa au matibabu ambayo umetumia katika wiki 2 zilizopita	Ndio Hapana	1 2	H3a
	Masharti maalum ya chakula	Ndio Hapana	1 2	H3b
	Ushauri au matibabu ya kupunguza uzito	Ndio Hapana	1 2	H3c
	Ushauri au matibabu ya kuacha kuvuta sigara	Ndio Hapana	1 2	H3d
	Ushauri wa kuanza mazoezi au kufanya mazoezi zaidi	Ndio Hapana	1 2	H3e
67	Je umeshawahi kupata ushauri au kutibiwa na mganga	Ndio Hapana	1 2	H4
68	Kwa sasa unatumia aina yoyote ya mitishamba kwa ajili ya shinikizo la damu	Ndio Hapana	1 2	H5

Historia ya Kisukari

Maswali		Jibu		Code
69	Umewahi kupimwa kiwango cha sukari katika damu?	Ndio Hapana	1 2	H6
70	Katika miezi 12 iliyopita, umewahi kuambiwa na daktari au mtaalamu mwingine wa afya kuwa una ugonjwa wa kisukari?	Ndio Hapana	1 2	H7a
71	Je umeambiwa hivyo ndani ya miezi 12?	Ndio Hapana	1 2	H7b
Magonjwa mengine				
72	Historia ya Ugonjwa wa kiharusi	Ndio Hapana Sijui	1 2 777	H8
73	Previous history of heart disease	Ndio Hapana Sijui	1 2 777	H9
Historia ya magonjwa sugu kwenye familia (Je kuna ndugu yeyote wa karibu; baba, mama, dada, kaka, au mtoto wako anayeugua au aliyewahi kuugua magonjwa yafuatayo?)				
74	Shinikizo la damu	Ndio Hapana Sijui	1 2 777	H10
75	Kisukari	Ndio Hapana Sijui	1 2 777	H11
76	Kiharusi	Ndio Hapana Sijui	1 2 777	H12
77	Ugonjwa wa moyo	Ndio Hapana Sijui	1 2 777	H13

Vipimo vya mwili visivyohusisha kutoa damu			
Urefu na Uzito		**Jibu**	**Code**
78	Utambulisho wa Mhojaji	⌊_⌊_⌊_⌋	M1
79	Utambulisho wa vifaa vya kupimia Urefu na Uzito	Urefu ⌊_⌊_⌋ Uzito ⌊_⌊_⌋	M2a M2b
80	Urefu	kwa Sentimeta(sm) ⌊_⌊_⌊_⌋ . ⌊_⌋	M3
81	Uzito *Ikiwa uzito umezidi uwezo wa mizani andika 666.6*	kwa Kilogramu (kg) ⌊_⌊_⌊_⌋ . ⌊_⌋	M4

82	***(Kwa Wanawake)*** Wewe ni mjamzito?	Ndio *1 Kama Ndio, nenda M 8* Hapana *2*	M5
Kiuno na mzunguko wa nyonga			
83	Utambulisho wa kifaa cha kupimia kiuno	⌊_⌋⌊_⌋	M6
84	Mzunguko wa Kiuno	⌊_⌋⌊_⌋⌊_⌋ . ⌊_⌋ cm	M7
85	Mzunguko wa Nyonga	⌊_⌋⌊_⌋⌊_⌋ . ⌊_⌋ cm	M8
Shinikizo la Damu			
86	Utambulisho wa Mhojaji	⌊_⌋⌊_⌋⌊_⌋	M9
87	Utambulisho wa kifaa cha kupimia BP	⌊_⌋⌊_⌋	M10
88	Ukubwa wa cuff itakayotumika	Ndogo 1 Ya kati 2 Kubwa 3	M11
89	Kipimo cha 1	SBP mmHg ⌊_⌋⌊_⌋⌊_⌋	M12a
		DBP mmHg ⌊_⌋⌊_⌋⌊_⌋	M12b
90	Kipimo cha 2	SBP mmHg ⌊_⌋⌊_⌋⌊_⌋	M13a
		DBP mmHg ⌊_⌋⌊_⌋⌊_⌋	M13b
91	Kipimo cha 3	SBP mmHg ⌊_⌋⌊_⌋⌊_⌋	M14a
		DBP mmHg ⌊_⌋⌊_⌋⌊_⌋	M14b
92	Katika wiki 2 zilizopita, umetumia dawa yoyote ya ongezeko la shinikizo la damu kama ulivyoandikiwa na daktari au mtaalamu mwingine wa afya?	Ndio 1 Hapana 2	M14
93	Mapigo ya moyo	Kipimo cha 1 ⌊_⌋⌊_⌋⌊_⌋	M16b
		Kipimo cha 2 ⌊_⌋⌊_⌋⌊_⌋	M16b
		Kipimo cha 3 ⌊_⌋⌊_⌋⌊_⌋	M16c
Vipimo vya mwili vinavyohusisha kutoa damu			
Sukari katika Damu		**Jibu**	**Code**
94	Ndani ya masaa 12 yaliyopita, umekula au kunywa kitu chochote zaidi ya maji?	Ndio 1 Hapana 2	B1
95	Utambulisho wa Mpimaji	⌊_⌋⌊_⌋⌊_⌋	B2
96	Utambulisho wa kifaa cha kupimia	⌊_⌋⌊_⌋	B3
97	Kiwango cha sukari katika damu kabla ya kula	mmol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B4

Vipimo vya Ziada			
Lehemu (Blood Lipids)			
98	Ndani ya wiki mbili je umekunywa dawa yeyote ya kupewa na daktari kwa ajili ya kushusha kiwango cha lehemu (cholesterol)	Ndiyo 1 Hapana 2	B5
99	HDL Cholesterol	mmol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B6
100	LDL Cholesterol	mmol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B7
101	Triglycerides *mmol/l*	mmol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B8
102	Total cholesterol*: mmol/l*	mmol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B9
(Vipimo vya Figo) Renal Function Tests and Urinary Albumin excretion			
103	Serum Creatinine	umol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B10
104	Urine Albumin	mg/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B11
105	Urine Creatinine	umol/l ⌊_⌋⌊_⌋ . ⌊_⌋⌊_⌋	B12

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