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ESTIMATING THE BURDEN OF SELECTED NON-COMMUNICABLE DISEASES IN AFRICA: A SYSTEMATIC REVIEW OF THE EVIDENCE

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DECLARATION

I, Davies O Adeloye, hereby declare that this thesis has been composed by me. The work included in the thesis is my own unless acknowledged otherwise. I certify that the work has not been submitted for any other degree or professional qualification except as specified.

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Date: 28 November 2014

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DEDICATION

To my wife, **Funke**.

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LAY SUMMARY

The burden of non-communicable diseases (NCDs), which cannot be transferred from one person to another, is rapidly increasing globally. Africa is particularly worst hit owing to rapid urbanization, population growth and ageing, and increased uptake of lifestyles associated with many NCDs, including tobacco smoking, alcohol consumption, sedentary lifestyles and increased consumption of food substances with high cholesterol and salts content. There is also poor data management and low level of research on many NCDs in Africa, and consequently, public health response has been suboptimal. This thesis focusses on understanding and estimating the prevalence, and/or where there are available data, the incidence, of major NCDs in Africa.

In 2010, about 130 million cases of hypertension were estimated in Africa, 58 million cases of asthma, 26 million cases of COPD, 25 million cases of diabetes, and 2 million cases of stroke. There were also about 496 thousand new cases of stroke. Among women, there were about 129 thousand new cases of cervical cancer and 81 thousand new cases of breast cancer. Among men, there were about 75 thousand and 74 thousand new cases of prostate cancer and Kaposi's sarcoma, respectively. These are relatively high estimates, which suggest that the burden of NCDs is growing in Africa. It is still not possible to state with all certainty how representative these estimates are, with regards to the entire African population. Without the availability of good data, research output my still be low and Africa may find it difficult to address this growing burden of NCDs. It is hoped that this research will prompt appropriate policy response across many countries in Africa.

ABSTRACT

Background

The burden of non-communicable diseases (NCDs) is rapidly increasing globally, and particularly in Africa, where the health focus, until recently, has been on infectious diseases. The response to this growing burden of NCDs in Africa has been affected owing to a poor understanding of the burden of NCDs, and the relative lack of data and low level of research on NCDs in the continent. Recent estimates on the burden of NCDs in Africa have been mostly derived from modelling based on data from other countries imputed into African countries, and not usually based on data originating from Africa itself. In instances where few data were available, estimates have been characterized by extrapolation and over-modelling of the scarce data. It is therefore believed that underestimation of NCDs burden in many parts of Africa cannot be unexpected. With a gradual increase in average life expectancy across Africa, the region now experiencing the fastest rate of urbanization globally, and an increase adoption of unhealthy lifestyles, the burden of NCDs is expected to rise. This thesis will, therefore, be focussing on understanding the prevalence, and/or where there are available data, the incidence, of four major NCDs in Africa, which have contributed highly to the burden of NCDs, not only in Africa, but also globally.

Methods

I conducted a systematic search of the literature on three main databases (Medline, EMBASE and Global Health) for epidemiological studies on NCDs conducted in Africa. I retained and extracted data from original population-based (cohort or cross sectional), and/or health service records (hospital or registry-based studies) on prevalence and/or incidence rates of four major NCDs in Africa. These include: cardiovascular diseases (hypertension and stroke), diabetes, major cancer types (cervical, breast, prostate, ovary, oesophagus, bladder, Kaposi, liver, stomach, colorectal, lung and non-Hodgkin lymphoma), and chronic respiratory diseases (chronic obstructive pulmonary disease (COPD) and asthma). From extracted crude prevalence and incidence rates, a random effect meta-analysis was conducted and reported for each NCD. An epidemiological model was applied on all extracted data points. The fitted curve explaining the largest proportion of variance (best fit) from the model was further applied. The equation generated from the fitted curve was used to determine the prevalence and cases of the specific NCD in Africa at midpoints of the United Nations (UN) population 5-year age-group population estimates for Africa.

Results

From the literature search, studies on hypertension had the highest publication output at 7680, 92 of which were selected, spreading across 31 African countries. Cancer had 9762 publications and 39 were selected across 20 countries; diabetes had 3701 publications and 48 were selected across 28 countries; stroke had 1227 publications and 19 were selected across 10 countries; asthma had 790 publications and 45 were selected across 24 countries; and COPD had the lowest output with 243 publications and 13 were selected across 8 countries. From studies reporting prevalence rates, hypertension, with a total sample size of 197734, accounted for 130.2 million cases and a prevalence of 25.9% (23.5, 34.0) in Africa in 2010. This is followed by asthma, with a sample size of 187904, accounting for 58.2 million cases and a prevalence of 6.6% (2.4, 7.9); COPD, with a sample size of 24747, accounting for 26.3 million cases and a prevalence of 13.4% (9.4, 22.1); diabetes, with a sample size of 102517, accounting for 24.5 million cases and a prevalence of 4.0% (2.7, 6.4); and stroke, with a sample size of about 6.3 million, accounting for 1.94 million cases and a prevalence of 317.3 per 100000 population (314.0, 748.2). From studies reporting incidence rates, stroke accounted for 496 thousand new cases in Africa in 2010, with a prevalence of 81.3 per 100000 person years (13.2, 94.9). For the 12 cancer types reviewed, a total of 775 thousand new cases were estimated in Africa in 2010 from registry-based data covering a total population of about 33 million. Among women, cervical cancer and breast cancer had 129 thousand and 81 thousand new cases, with incidence rates of 28.2 (22.1, 34.3) and 17.7 (13.0, 22.4) per 100000 person years, respectively. Among men, prostate cancer and Kaposi sarcoma closely follows with 75 thousand and 74 thousand new cases, with incidence rates of 14.5 (10.9, 18.0) and 14.3 (11.9, 16.7) per 100000 person years, respectively.

Conclusion

This study suggests the prevalence rates of the four major NCDs reviewed (cardiovascular diseases (hypertension and stroke), diabetes, major cancer types, and chronic respiratory diseases (COPD and asthma) in Africa are high relative to global estimates. Due to the lack of data on many NCDs across the continent, there are still doubts on the true prevalence of these diseases relative to the current African population. There is need for improvement in health information system and overall data management, especially at country level in Africa. Governments of African nations, international organizations, experts and other stakeholders need to invest more on NCDs research, particularly mortality, risk factors, and health determinants to have evidenced-based facts on the drivers of this epidemic in the continent, and prompt better, effective and overall public health response to NCDs in Africa.

1 INTRODUCTION

1.1 OVERVIEW

In the last two decades, the burden of diseases in Africa has been tagged '*double burden*'. This term refers to the burden of diseases in Africa due to the dual effects of the already present high burden of communicable (infectious) diseases and a growing burden of non-communicable diseases (NCDs) (Boutayeb, 2006). The health focus in Africa, until recently, has been on communicable diseases, notably HIV/AIDS, malaria and tuberculosis, with minimal attention on NCDs (Dalal et al., 2011). The burden of NCDs in Africa, having presumably gone unnoticed over the years, has gradually become a major public health concern (Boutayeb, 2006, Amuyunzu-Nyamongo, 2010). The World Health Organization (WHO) news release explained that NCDs are on the increase, that they became the leading killer diseases today and have caused a two-punch blow to global development (World Health Organization, 2011b).

The burden of non-communicable diseases (NCDs) is rapidly increasing globally (World Health Organization, 2008). The 2011 United Nations (UN) high level political meeting on NCDs affirmed that NCDs jointly became the leading cause of deaths globally, and are expected to account for about 52 million deaths by the year 2030 (United Nations, 2011, Beaglehole et al., 2011). Evidence suggests that this global increase in NCDs burden over the last two to three decades may be due to the fact that awareness and health response at global levels have been weighted towards infectious disease than NCDs (Beaglehole et al., 2011). For example, a review of World Health Assembly (WHA) resolution from 1948 to 2013 revealed that of the total 484 resolutions made by WHA, 368 (76.0%) were on infectious diseases, 99 (20.5%) on NCDs and 17 (3.5%) on both (World Health Organization, 2014e, World Health Organization, 2014d). Meanwhile, the WHO and many stakeholders have in recent times turned towards addressing NCDs burden more keenly, especially in Africa and many low- and middle-income countries (LMIC), where infectious diseases still remain a large public health issue (World Health Organization, 2008). In 2012, the World Health Assembly endorsed a new health goal (the "25 by 25

goal"), mainly focussing on reduction of avoidable deaths from non-communicable diseases (NCDs) by 25% by the year 2025 (Horton, 2013). Experts have again lauded this as a step in the right direction, especially after the 2011 UN political declaration on control and prevention of NCDs (Bonita et al., 2013). However, according to Horton, there are lots of obstacles (local, regional and global) that have prevented this goal and many other initiatives on NCDs from being achieved, which has thus constrained the ability of many stakeholders to transform their understandings of the NCDs burden into political action (Horton, 2013).

Records show that Africa is currently experiencing the fastest rate of urban development and industrialization worldwide (Mufunda et al., 2006b). Consequently, with increasing living standards and better healthcare seeking across many African countries, life expectancy will continue to rise (Ezzati et al., 2003). Therefore, the fast rising burden of NCDs in Africa could be partly due to demographic changes or population dynamics, including migration and ageing of the population, and partly to rapid industrialization and adoption of urban lifestyles (Lim et al., 2012). These two are jointly the main drivers of the pandemics of NCDs in Africa. In the absence of effective interventions and control measures, they are likely to increase both the prevalence and the total number of cases for many NCDs across Africa in the near future (Beaglehole, 2011).

What does the term "burden" imply in this context?

Generally, burden of disease can be described as a measure employed in assessing the health impact of different diseases (including injuries) on a defined population (Bloom et al., 2011). Assessing the burden of disease may involve the following:

i. *Measuring the occurrence of a disease in a population*: This involves estimating the number of people with a disease in a population. It is usually expressed as *incidence* or *prevalence*. These are further explained below.

ii. *Measuring deaths from a disease in a population*: The number of deaths resulting from a particular disease is another measure of disease burden. This

may be expressed as *mortality rate*, *case fatality rate*, among others. These are also explained further below.

iii. *Measuring risk factors associated with a disease in a population*: A risk represents the probability of the occurrence of a health outcome or an event (e.g. risk of having a disease or risk of dying from a disease) in a defined population (Alwan et al., 2010). In other words, a risk may be described as an aspect of an individual's characteristics, inherited feature, lifestyle, and/or environmental exposure that is associated with an increased probability of occurrence of a disease (Kamadjeu et al., 2006). Some risk factors may be modifiable, and intervening to alter these risk factors may reduce the occurrence of disease/s they are associated with. Specifically for NCDs, tobacco smoking, harmful use of alcohol, unhealthy diet and physical inactivity have been described as the four major risk factors (Boutayeb, 2006). This is explained further under *section 1.1.5- risk factors*.

iv. *Measuring the socio-economic impact or financial cost of a disease in a population*: This is another measure of disease burden that describes the social, economic, and financial impact of disease in a population (Schneider et al., 2009). In some instances, an assessment of the socio-economic burden has been applied by governments to make vital policy decisions on a disease (Boutayeb, 2006, Bloom et al., 2011). This is further explained under *section 1.1.4- socio-economic burden*.

Meanwhile, in the last two decades, burden of disease has been described in terms of years of healthy lives lost due to a particular disease, and years lived with disability as a result of the disease (Murray and Lopez, 1996). The above are all measures of different elements of the overall burden of disease. The use of each (i.e. incidence, prevalence, mortality rate, CFR, risk factors or assessment of socio-economic burden of a disease) may depend, among many others, on what has already been measured on the disease, feasibility and cost effectiveness of embarking on such measures of disease burden, what interventions are being targeted and how such measures of

disease burden (when reported) may positively influence healthy public decisions and policies.

In estimating the burden of disease, one fundamental step is to appropriately define the disease following agreed or standard case definitions. This generally requires standard clinical criteria to be met (which may include the use of standard tests) to meet internationally agreed case definitions (Burney et al., 1989). Thus, during epidemiological surveys, it may not be sufficient to count the number of locally recorded disease cases, rather, counting the number of people that meet internationally agreed case definitions is required (Trepka et al., 2009). A major limitation, which was observed in this thesis, is that case definitions are often imperfect and not applied consistently in all studies.

As noted above, measuring the occurrence of a disease in a population may involve measurement of prevalence and/or incidence rates of the disease. In simple quantitative terms, prevalence is defined as the number of persons with a disease divided by the total number of people assessed for the presence of disease (Kamadjeu et al., 2006). While this has been described as a useful epidemiological measure to inform policy decisions (in that, it is a simple straightforward measure of the number of people living with a disease (Alwan et al., 2010)), it has a number of important limitations. These include problems with case definitions, variable degrees of proper application of standard protocols, sampling errors, problems of incomplete data due to low levels of voluntary participation in the prevalence survey, challenges arising from those with positive history of the disease but who do not have identifiable disease at the time of survey, and problems arising due to imperfect sensitivity and specificity of survey methods, leading to over- or under-estimation of the disease (Alwan et al., 2010). *Point-prevalence* is simply the number of people with identifiable disease at a particular point in time; *period-prevalence* is the number of people with identifiable disease over a period of time; and *lifetime-prevalence* is the number of people who have or have had the disease at any point in their life. One of the major challenges encountered in conducting systematic reviews of prevalence

studies is that studies use different prevalence measures and sometimes do not make it clear which measure they are reporting.

Incidence introduces the concept of time into disease measurement (Chokunonga et al., 2000). It is usually measured in prospective longitudinal studies, where all people in the study are assumed to be healthy at the start of the survey (with attempts made to exclude people with prevalent disease) and are followed up over a period of time to detect new cases of the disease (Arbyn et al., 2011). It is calculated as the number of new cases of a disease divided by total number of persons at risk over the follow-up period (Chokunonga et al., 2000). It is, however, important to have an appropriate understanding of the study population and its age and gender distribution to allow for appropriate comparisons with other population groups. This is particularly important when seeking to make summary estimates in systematic reviews.

Deaths from diseases are measures of disease burden that are commonly expressed as mortality or case fatality rates (Walker et al., 2013). Mortality can be defined just like incidence but with the numerator having *deaths* in place of *new cases* of the disease (Danesi et al., 2013). Mortality rate is calculated as the number of deaths from a disease occurring in a population over a particular period divided by the total number of persons at risk of dying during this period (Walker et al., 2013). Crude mortality rate describes deaths from all causes, while disease-specific mortality rate only covers deaths due to one disease (Walker et al., 2013, Danesi et al., 2013). Meanwhile, case fatality rate (CFR) is based on numbers of deaths and total incident cases. It is defined as the proportion of incident cases that die within a specific time period, or the proportion of deaths within a defined population of incident cases measured over the course of the disease (Danesi et al., 2013, Murray and Lopez, 1996). CFR is commonly applied to a specific outbreak of acute disease in a population in which all affected cases have been followed for an adequate period of time to include all deaths due to the disease (Danesi et al., 2013). Again, many of the challenges highlighted under prevalence studies may also be encountered here.

As noted above, in recent times, the Institute of Health Metrics Evaluation (IHME) has developed alternative measures to estimate the burden of disease (Lozano et al.,

2012, Murray et al., 2012). This is mainly expressed in the form of disability adjusted life years (DALYs). DALY is defined as the sum of years lived with disability (morbidity) and years of healthy life lost due to premature mortality (Murray and Lopez, 1996). This is discussed further in the next section.

Understanding the concept of DALYs and YLL in the estimation of disease burden

In the early 1990s, the concept of DALYs gradually became a widely accepted metric in the measure of disease burden (Murray and Lopez, 1996). According to Murray and Lopez, the DALYs philosophy was to provide a summary measure of disease burden for public health use by combining morbidity, mortality, disease occurrence and severity in an estimation model (Murray and Lopez, 2013). Murray and Lopez further stated that this approach was necessary to inform health priority setting, health research priority setting, and identification of disadvantaged groups to be targeted with health interventions. It also provided a metric for use in evaluations of interventions and health programmes and in planning exercises (Murray and Lopez, 2013). The first study of the global burden of disease using DALYs was conducted in 1990. This study quantified the health effects of over a hundred diseases and injuries for eight regions of the world. As noted in the preceding section, a DALY is expressed mathematically as:

$$1 \text{ DALY} = \text{YLD} + \text{YLL}$$

where YLD = Years Lived with Disability (morbidity)

$$1 \text{ YLD} = \text{Number of cases} * \text{Duration} * \text{Disability Weight}$$

and YLL = Years of Life Lost due to premature mortality (mortality)

$$1 \text{ YLL} = \text{Number of deaths} * \text{Life Expectancy at Age of death}$$

(Murray and Lopez, 2013, Murray and Lopez, 1996).

Concerns have been raised by some health experts over how equitable these disability weights (and/or age weightings) are, and whether they also take into consideration comparability between countries and regions (Anand and Hanson, 1998, Anand and Hanson, 1997). These weightings may reflect more the

understanding of researchers and the baseline estimation methods may not be applicable to all countries. Another issue which has been raised is the extent to which a "*true*" life expectancy table has been developed and to what extent age and gender have been equally considered in this approach (Anand and Hanson, 1997).

Aside from these methodological issues, DALYs have been described as a complex simplification of reality, and may only give a crude indication of disease burden. DALYs have been thought not to capture other aspects of disease pathways, including pain, depreciating quality of life, and emotional, physical and psychological trauma (World Health Organization, 1996). Additionally, with a widely accepted use of DALYs in the estimation of disease burden, it is possible that donors may have directed their funds (on a very large scale) at diseases with high DALYs in a particular region, while ignoring the fact some diseases with lower DALYs in this region may still be a major cause of disease burden in some other world regions (Steenland and Armstrong, 2006).

Notwithstanding these criticisms, it is important to state that the recent IHME GBD estimates (the Global Burden of Disease 2010 (GBD-2010)) are still regarded as one of the largest epidemiological assessments of global data on health ever conducted (Lim et al., 2012, Lozano et al., 2012, Murray et al., 2012). Some of the major limitations (some of which were first identified in the 1990s when DALYs was introduced (World Health Organization, 1996)) are briefly discussed in the next section.

Limitations of IHME methods and estimation

Experts have described DALYs mainly as an aggregate measure of health status, and may not be closely (and/or truly) representative of country or regional estimates (World Health Organization, 1996). The estimates attempt to characterize loss of health from diseases and injuries, while also assessing the role of major risk factors across many world regions (Murray and Lopez, 2013). This approach has tended to give insufficient attention to obvious country and regional heterogeneities and so much useful information may actually be hidden. Byass and colleagues critically appraised the GBD 2010 study and reported that estimates should be clearly regarded

as estimates, and by no means described as actual measurements (Byass et al., 2013b).

Concerns have been raised among experts on the source/s of data from which these estimates are derived, especially for the GBD 2010 study (Byass et al., 2014, World Health Organization, 1996). IHME did report that data were derived from a mixture of vital registration, sample registration and survey data (Murray and Lopez, 2013). The question is where exactly were these data sourced from and why were they not made publicly available? In this thesis, access to these data sources could have allowed direct comparisons and possible corroborates to be made with the reported estimates.

Another limitation of the IHME approach is that available data are not sufficient to support valid and precise large estimates on all diseases, injuries and risk factors across all world regions (World Health Organization, 1996). In the view of many commentators, these estimates are a product of sophisticated modelling of sparse and inconsistent data (Byass et al., 2014, World Health Organization, 1996). Vital registration currently covers about 40% of global deaths, with many of these coming from regions with incomplete, passive and irregular vital registration (Byass et al., 2014, Murray and Lopez, 2013). In addition, many diseases and deaths occur in rural areas worldwide, especially in Africa, with most of these occurring without any record (Byass et al., 2014). This raises concerns about the level of coverage and completeness of underlying mortality data, especially from low income countries. This also affects the uncertainty intervals of the estimates reported. Byass and colleagues reported that the IHME 95% uncertainty intervals were also complex and only reflected uncertainty from the modelling employed rather than due to the quality and number of data sources. For example, in regions where data were largely unavailable, the uncertainty intervals should be relatively wider than in other world regions with more detailed data to reflect this lack of data (Byass et al., 2013b).

In general, many IHME data sources are unavailable and data from many parts of the world are incomplete, leading to reported estimates which may be more a product of complex modelling than a true reflection of the true burden of disease. Dr Margaret

Chan, the WHO Director General, explained that to arrive at population representative figures of the global, regional and country estimates of disease burden, the focus should now be on closing data gaps, especially across many low-and middle-income countries. If this were achieved, then the need for complex statistical modelling for burden of disease estimates would become less necessary (Chan, 2012).

Why is my approach different from the IHME methods?

A general concern is that in Africa, vital registration systems and health management information systems can be said to be in a developmental state, and too incomplete to provide the data needed (Byass et al., 2014). Indeed, in many parts of Africa, health management information systems are virtually non-existent (Byass et al., 2014). The data that are available in some African sub-regions tend to be mainly on causes of deaths and not on disease prevalence or incidence. Moreover, IHME has been working more on deaths (and DALYs) over the last two decades, and many concerns have been raised over their estimates. The sources of IHME data have also not been made publicly available, thus estimating other measures of disease burden, including prevalence and/or incidence, from their published data is often not possible.

In terms of the stakeholders in the health sector across many parts of Africa, understanding of the epidemiology of NCDs in Africa is presently quite poor due to the lack of data and low level of research on NCDs (King and Bertino, 2008). Africa has recently seen a large increase in life expectancy and urbanization, which has been driving an increase in the NCD burden in the continent (Assah et al., 2011). Many studies reporting the burden of NCDs in Africa are derived, at least in part, from modelling based on data from other countries imputed into African countries, and may not be strictly based on data originating from Africa itself (Kirigia and Barry, 2008). This is therefore in stark contrast with the need to have useful local information on NCDs, with particular focus on data derived from Africa, as recommended in the UN's approach to the political prioritization of the NCD burden (Beaglehole et al., 2011). There are also reports that African leaders and policymakers may be more interested in knowing the actual number of people living

with a disease (i.e. the prevalence or incidence) to inform policy decision-making. This may partly reflect the fact that the concept of DALYs, widely reported by IHME, are not widely understood (King and Bertino, 2008, Kirigia and Barry, 2008).

Thus, based on this understanding, and with the already extensive estimates of DALYs and deaths on many diseases in Africa reported by the IHME, I decided to focus on estimating the prevalence and/or incidence of major NCDs in the African continent (discussed in *Section 1.1.7*). To address some of the concerns raised by experts on the IHME estimates, I conducted a thorough systematic search of literature. The data sources and all data points were clearly presented and made publically available (see also **Appendix**). Second, to address the concern about complex modelling applied on scarce data from the African region, a simple meta-regression epidemiological model was applied on all data based on reported mean age from each study (since this was the main available confounding factor for which data were available in most studies). However, this still does not imply that estimates presented in this thesis are without limitations. A range of limiting factors is presented and discussed in the discussion section (*Section 1.1.3*).

1.1.1 The Global Burden of Non-Communicable Diseases

In 2008, according to the WHO global burden of disease (GBD) estimates, NCDs accounted for about 36.1 million deaths in the world (63% of global deaths) of which 80% occurred in low- middle-income countries. They have been projected to account for about 52 million deaths by 2030 (World Health Organization, 2011b). Cardiovascular diseases (CVDs) ranked highest, accounting for 17 million deaths (48% of global NCDs deaths). Cancer accounted for 7.6 million deaths (21% of global NCDs deaths), chronic respiratory diseases (CRDs) 4.2 million deaths (11.7% of global NCDs deaths) and diabetes 1.3 million deaths (3.5% of global NCDs deaths) (**Table 1.1**) (World Health Organization, 2008). These four diseases, according to WHO records, account for almost 80% of global deaths from NCDs (World Health Organization, 2008). Interestingly, they are associated with four shared risk factors: tobacco use, physical inactivity (or sedentary lifestyle), harmful

use of alcohol and unhealthy diets (World Health Organization, 2011a). According to WHO 2008-2013 Action Plan for the Control of NCDs, about 80% of cardiovascular diseases, type 2 diabetes and over a third of cancers could be prevented by eliminating these shared risk factors (World Health Organization., 2007).

Table 1.1. Distribution of the leading global NCD deaths by WHO regions in 2008

WHO region	*Cancer*		*Cardiovascular*		*Diabetes*		*Chronic Respiratory*	
	Deaths (in millions)	*% of global NCD deaths*	*Deaths (in millions)*	*% of global NCD deaths*	*Deaths (in millions)*	*% of global NCD deaths*	*Deaths (in millions)*	*% of global NCD deaths*
Global	7.6	21.1	17.3	48.0	1.3	3.5	4.2	11.7
Africa	0.4	1.1	1.3	3.5	0.2	0.5	0.3	0.9
The Americas	1.2	3.3	1.9	5.4	0.3	0.8	0.4	1.1
Eastern Mediterranean	0.3	0.9	1.2	3.3	0.1	0.2	0.2	0.4
Europe	1.9	5.2	4.6	12.7	0.2	0.4	0.4	1.0
South-East Asia	1.1	3.1	3.6	10.0	0.3	0.8	1.4	3.8
Western Pacific	2.7	7.4	4.7	13.1	0.3	0.7	1.6	4.4

Source: WHO Global Burden of Disease 2008 (World Health Organization, 2008)

The 2010 Institute of Health Metrics Evaluation (IHME) GBD estimates confirmed many reports on the increase of NCDs globally. In 1990, there were 46.5 million deaths from all causes globally, with NCDs accounting for 26.6 million (57.1% of global deaths), while of the 52.8 million global deaths from all causes in 2010, 34.5 million (65.3% of global deaths) were attributable to NCDs (Lozano et al., 2012). On the measure of disabilities, there were a total of 2502.6 million DALYs in 1990 and 1075 million (43% of global DALYs) was attributable to NCDs; this percentage was also relatively lower compared to a total of 2490.4 million DALYs and 1343.7 million (54% of global DALYs) attributable to NCDS in 2010 (Murray et al., 2012), see **Table 1.2**.

Table 1.2. Distribution of the leading global NCD deaths and DALYs in 1990 and 2010

NCDs	*1990*		*2010*		*1990*		*2010*	
	Deaths (millions)	***% of global deaths***	***Deaths (millions)***	***% of global deaths***	***DALYs (millions)***	***% of global DALYs***	***DALYs (millions)***	***% of global DALYs***
Total	26.6	57.1	34.5	65.3	1075.3	42.9	1343.7	53.9
CVDs	11.9	25.6	15.6	29.5	240.7	9.6	295.0	11.8
Cancers	5.8	12.5	7.98	15.1	148.1	5.9	188.5	7.6
CRDs	3.99	8.6	3.8	7.2	119.2	4.8	117.9	4.7
Diabetes	0.7	1.5	1.3	2.5	27.8	1.1	46.8	1.9

Source: (Lozano et al., 2012, Murray et al., 2012)

1.1.2 The State of Non-Communicable Diseases in Africa

The current global estimates reveal that NCDs mortality is higher than mortality that is attributable to other causes in all region of the world except in Africa. However, records still show that age standardized NCDs mortality rates were the highest in Africa in 2008 (males- 844/100000 and females- 724/100000), and a 20% increase in mortality has been projected by 2030 (World Health Organization, 2011a).

According to the WHO GBD estimates, NCDs are the second leading cause of death in the African region (World Health Organization, 2008). Across Africa, NCDs accounted for 30% and 25.8% of the overall 9.5 million deaths and 675.4 million DALYs recorded in Africa in 2011 (World Health Organization, 2014b). It was estimated that cardiovascular diseases accounted for 10% of all deaths in the region, with cancer accounting for 4%, CRDs for 3%, and diabetes for 1% (World Health Organization, 2014b). In exact quantitative terms, CVDs accounted for 1.3 million deaths (3.5% of global NCDs deaths), followed by cancer, accounting for 0.4 million deaths (1.1% of global NCDs deaths), CRDs, for 0.3 million deaths (0.9% of global NCDs deaths), and diabetes, for 0.2 million deaths (0.5% of global NCDs deaths)

(World Health Organization, 2008), see **Table 1.1**. In this thesis, these four major NCDs (CVDs, diabetes, cancer and CRDs) will be the main focus.

Across African sub-regions, the burden is particularly higher in North Africa compared to sub-Saharan Africa (World Health Organization, 2011c). For example, the 2008 WHO estimates showed that NCDs accounted for 82% of all deaths in Egypt, 75% in Morocco, 63% in Algeria, 78% in Libya and 72% in Tunisia, while countries like Nigeria had NCDs mortality of about 27% of all deaths, Ghana 39%, Kenya 28%, Uganda 25%, and Zimbabwe 21% (World Health Organization, 2011c). Meanwhile, in 2000, the burden of NCDs in South Africa was estimated to account for about 21% Years of Life Lost (YLL) (Bradshaw et al., 2003). Recent studies show that death rates from NCDs in South Africa have actually increased from what was observed in 2000, accounting for 29% of all deaths in South Africa in 2008 (almost the same range with figures in other sub-Saharan countries) (World Health Organization, 2011c).

Meanwhile, the increasing trend of NCDs in Africa is thought to be partly due to population dynamics and demographic transitions occurring at a faster rate in Africa in comparison to many developed countries, and this not allowing for effective adaptation period in many African countries (Kengne and Mayosi, 2014). The differences in the capacity of African countries to effectively respond to the NCDs surge have also been a factor (Kengne and Mayosi, 2014). According to the WHO, emerging evidence suggests that NCDs is increasingly receiving the needed attention across Africa, with about 89% of African countries having a dedicated unit for NCDs within their national ministry of health (World Health Organization, 2011c). Nevertheless, looking at specific NCDs response, reports show that only 26% of African countries had a functional programme for anyone of the four major NCDs (CVDs, diabetes, cancer and CRDs) in Africa (World Health Organization, 2011c). In the absence of a concerted continent-wide intervention, WHO projects that the greatest increase in NCDs deaths will occur in the African region (27%) in the next decade, with NCDs exceeding infectious diseases as the most common cause of death in the region by 2030 (World Health Organization, 2008).

1.1.3 Heterogeneities within and between African population groups

One important issue in estimating the burden of any disease is to arrive at estimates that are closely representative of the population under study, while considering a host of inherent demographic factors. In Africa, this may appear difficult to achieve owing to wide heterogeneities within and between population groups. This was therefore a major challenge for this thesis, as the few studies included in the thesis had varying degrees of heterogeneities, mostly due to differences among the population groups. The estimates should therefore be interpreted with caution. Meanwhile, urbanization, age, ethnicity, and gross domestic product (GDP) across Africa, and their associations with the risk factors for some NCDs will be briefly examined in this section in order to have a background understanding of these heterogeneities.

Urbanization

To fully understand heterogeneities in the African population with regards to urban versus rural dwellers, it is worthwhile to briefly mention the epidemiological transition in the African context. According to WHO, more than 100 countries worldwide are transitioning rapidly towards a greater percentage of deaths from NCDs and injuries, and this is now most pronounced in Africa (World Health Organization, 2011c). Reports show that the rate of urbanization, ageing and adoption of western lifestyles is fastest globally in the African continent (Apt, 2004, Assah et al., 2011). This has obviously resulted in a gradual reduction in the importance of infectious diseases and nutritional deficiencies (which are common in childhood) and increase in the importance of NCDs (Stern et al., 2010). Epidemiological transition is basically associated with industrialization and development, and involves the overall process by which patterns of risk factors, disease mortality and morbidity shifts over time (Assah et al., 2011).

Over 530 million people reside in rural areas in sub-Saharan Africa (BeLue et al., 2009). Studies have shown that between 1970 and 1982, African urban populations grew by about 6% per year, and between 1990 and 2010, this rate nearly doubled (BeLue et al., 2009). It is believed that rates of occurrence of NCDs tend to be much

lower in rural settings compared to urban settings (Assah et al., 2011). But as noted above, many of these rural settings are rapidly becoming urbanized (although it is important to note that the rate of urbanization is likely to differ markedly between different countries in Africa) (Niakara et al., 2007). Indeed, it is now difficult to strictly assign an area as a predominantly rural setting (Niakara et al., 2007). Meanwhile, authors have warned that rapid urbanization in many parts of Africa is an important psychological stressor among urban dwellers, This is due, for example, to the creation of mega-slums with attendant deterioration in health and well-being, especially due to poor housing, sanitation, and unaffordable and limited access to health services (BeLue et al., 2009). Many studies have further shown that hypertension, obesity, sedentary lifestyle, high salt and fats intake, smoking and alcohol consumption are major NCD risk factors commonly associated with urban dwellers (Niakara et al., 2007, Sobngwi et al., 2002, Mbanya et al., 2010). Thus, attention to the differing characteristics of urban or rural settings (as an important issue which can create heterogeneities) need to be carefully considered in any African study, as an inappropriate classification of these may affect the overall interpretation of findings of the study.

Age

Increasing age is a major risk factor for many NCDs (Abegunde and Owoaje, 2013). Many studies have reported that the prevalence rates of hypertension, stroke, COPD and cancer increase with increasing age (Abegunde and Owoaje, 2013, Ejim et al., 2011, Ezenwaka et al., 1997, Hammami et al., 2011). It therefore forms an important heterogeneity that needs to be carefully considered across various African populations. According to the United Nations, Africa's population was estimated at 967 million in 2008, with about 42% aged below 15 years (United Nations, 2013). Experts believe this relatively youthful population thus provides a drive for population growth in the region with an annual growth rate of 2.4% (Abegunde and Owoaje, 2013). Africa has the youngest population worldwide, with a median age of 19.7 years in 2012 (United Nations, 2013). Currently, about 85% of the African population are below 45 years of age and only 5% are aged 50 years and above

(BeLue et al., 2009). The significance of this is that when a predominantly young population in Africa continuously gets exposed over time to NCD risk factors (and carry the consequences of this exposure into adulthood) a greater percentage of adults in the productive age group in the continent (15-60 years) may be living with NCDs in the next two to three decades. One can also expect that premature mortality from NCDs in the region may be relatively higher than in other parts of the world.

Additionally, at a time when the average global life expectancy was estimated to be 73 years (in 2013), the average life expectancy at birth in Africa was 59 years, with 9 African countries having life expectancies less than 55 years (World Bank, 2014b). Across individual African countries, Liberia, Ethiopia and Rwanda had the highest increase in life expectancy in Africa between 1990 and 2013 (increases being 42 to 62 years, 45 to 64 years, and 48 to 65 years, respectively) (World Bank, 2014b). If this rapid increase in life expectancy in these three countries is maintained over the next two to three decades, one may expect a relative increase in the proportion of the population in the older age groups than observed presently, and consequently the prevalence of NCDs in the older age groups can be expected to increase.

Among African population groups, age may become a factor with regards to place of residence. Across many African countries, there is a rapid efflux of young and educated age groups from rural areas to urban centres in search of a better livelihood (Stern et al., 2010). In the meantime, this may imply that the population in urban centres comprise a mix of rural and urban dwellers. Therefore, the observed disease patterns in these settings in any study may need to be cautiously interpreted. While over time, rural centres may become depleted and the older age groups left behind may actually be lacking the needed healthcare (especially care related to emotional and family ties) (BeLue et al., 2009). This may lead to some degrees of depression, dementia and some psychological disorders in the elderly population.

Ethnic diversity

Africa is made up of enormously diverse groups of people in terms of ethnicity, racial grouping, culture and language (Mathenge et al., 2010). The ethnic groups in Africa number in thousands and each of these have a specific culture and way of life,

which can be linked with their health behaviours (Mathenge et al., 2010). Therefore, cultural and ethnic diversity is an important part of health research that needs to be well understood in the estimation of disease burden. In fact, a thorough situation analysis aimed at understanding the cultural context in which diseases are interpreted and responded to by a community is vital to developing lifestyle and behavioural modifications that can be easily accepted by the community (BeLue et al., 2009). A typical example is in the interpretation of diabetes symptoms. The Akan ethnic group in Ghana refer to diabetes as sugar disease in Twi language (de-Graft Aikins et al., 2010a); diabetes is referred to as disease with *sugary urine and cluster of ants* in Yoruba tribe in Nigeria (Oladapo et al., 2010); and in a separate study of 72 patients with diabetes, native labels for diabetes translated into *sugar sick* or *illness that originates from too much sweet things* (Mbanya et al., 2006).

The cause of disease in many African ethnic groups has been attributed to witchcraft, punishment from gods, and poverty, among others (Assah et al., 2011). This may also influence the increased patronage of traditional and faith healers, as many of these healers are presumed to be able to tackle these causes (BeLue et al., 2009). They therefore offer "*cure*" for some NCDs (like diabetes and hypertension) based on this understanding and from the fact that many patients cannot afford care from expensive standard health facilities (BeLue et al., 2009). In fact, some communities now believe that herbal concoctions and home-brewed beer are the best treatment for hypertension and diabetes (Koopman et al., 2012).

Meanwhile, the prevalence of some diseases is common to some specific ethnic groups in Africa. For example, among East Africans, oesophageal cancer is thought to be more common (the reasons for this not fully understood), while hypertension and stroke is less common (possibly due to intense physical activity in these region) (Madebo et al., 1994). In West Africa, the Fulani ethnic group are traditional nomadic pastoralists and research in this group shows they have low cardio-metabolic risk, possibly due to the long hours each day spent walking (Oladapo et al., 2010).

These are examples of the cultural and ethnic diversities that need to be well understood in the estimation and interpretation of disease burden data.

Gross Domestic Product (GDP)

Reports have shown that GDP and the average income status in a country may affect the occurrence of disease (Stanciole et al., 2012). Many chronic diseases have been said to be relatively high in Northern parts of Africa due to the better standards of living in these countries, as western lifestyles including smoking, alcohol consumption, sedentary lifestyles and high intake of salts and fats are relatively common (Nejjari et al., 2013). On the average, Northern African countries have a higher GDP than in other parts of Africa, with Egypt having a GDP of US$229.5, Algeria US$188.7, Morocco US$100.2, Libya US$62.4 and Tunisia US$45.9 billion, respectively, in 2013 (World Bank, 2014b).

In Central, East and West African regions, however, the standard of living is lower with the percentage of the population living on less than US$2 per day reported at about 50% or more in every country (World Bank, 2014a). The increase in the burden of NCDs in these regions has been linked mostly to inability to access and afford standard health services (Stanciole et al., 2012). Sao Tome & Principe, Guinea Bissau, Gambia and Liberia have the some of the lowest GDPs in the African region, at US$0.2, US$1.0, US$1.1, US$1.2 billion, respectively, in 2013 (World Bank, 2014b).

In terms of country level GDPs in Africa, Nigeria and South Africa stand out as the two highest GDPs in Africa in 2013 at US$509.9 and US$408.2 billion, respectively (World Bank, 2014b). Indeed, economic activity in many sub-Saharan African countries was robust in 2013 with a GDP growth strengthening from 3.7% in 2012 to 4.7% in 2013 (World Bank, 2014a). There has been very encouraging investment in infrastructure, including those related to health services (Stanciole et al., 2012). However, across many African countries, the effects on health are yet to be appreciated due to the negative influences of poor leadership, managerial ineptitude, corruption, and inequity in the distribution of resources (World Bank, 1993). GDP has been described as an important underlying determinant of the prevalence of

many chronic diseases. The main socio-economic stressors include unemployment, illiteracy, unstable power supply, and lack of potable water (World Bank, 2014a).

In the next section, the socio-economic burden of NCDs will be examined.

1.1.4 Socio-Economic Burden

It has been observed that approximately 30% of deaths from NCDs in low- and middle-income countries occur in people younger than 60 years, which are actually a productive age group, thus bearing down heavily on socioeconomic status, the already stretched health systems and government finances, and family budgets in these regions (Clark, 2013).

Studies have shown that NCDs and poverty may be mutually related (Schneider et al., 2009). NCDs, in the presence of other social determinants of health, have pushed millions of people below the poverty index with many living below a daily income of $1.25 per day in Africa (de-Graft Aikins et al., 2010b). Dr Margaret Chan states that billions of United States dollars (USD) were lost across many countries in 2008 due to NCDs owing to huge costs incurred by various national health systems (World Health Organization, 2008). It has also indirectly affected the United Nations Millennium Development Goals (UN MDGs), where MDGs 2, 4 & 5, which addresses poverty, maternal and child health have been difficult to achieve, especially in resource-poor settings (World Health Organization, 2011b).

In financial terms, NCDs were estimated in 2005 to cost $18 billion in China, $9 billion in India and $3 billion in Brazil. Cost analysis of NCDs burden in Africa was estimated in 2005 and projected to increase by over 30% in 2025, based on the health expenditure in China, India and Brazil (World Health Organization, 2011a). For example, the estimated average annual cost of managing diabetes (which is known to interact with many NCDs) in sub-Saharan Africa is $8836 per patient (Hall et al., 2011). In-depth analysis based on the total African population has shown that this figure by Hall and colleagues corroborates with the NCDs cost estimates reported for Africa (Hall et al., 2011, Asaria et al., 2007).

1.1.5 Risk Factors

The risk factors noted above (smoking, harmful use of alcohol, sedentary lifestyles and unhealthy diets) are actually behavioural risk factors, which could lead to any of the metabolic risk factors (increased blood pressure, plasma glucose, cholesterol, and body mass index (BMI)).

Tobacco use

According to the WHO, tobacco use accounts for over 9% of global deaths (World Health Organization, 2008). Studies show that Africa actually has the lowest smoking rate in the world with about 8% of over 1 billion smokers in the world (World Health Organization, 2011c). However, Africa has recently become a potential market target for tobacco manufacturers, thus there has been some increase in consumption in Africa in the last five years (Kengne et al., 2007). According to WHO GBD estimates, smoking is known to cause about 71% of all lung cancers, 42% of chronic respiratory diseases and 10% of CVDs (World Health Organization, 2008).

Alcohol

Harmful use of alcohol accounts for about 2.3 million deaths per year (World Health Organization, 2008). Alcohol consumption is largely responsible for many cancers, cardiovascular diseases and liver diseases. Studies show that alcohol consumption is gradually increasing in Africa, as people now consume it on the assumption that low-risk pattern of alcohol consumption could be beneficial (Kengne et al., 2007).

Diet

Unhealthy diets and poor nutrition are very prevalent in Africa, and the relatively low income status and standards of living have been implicated (Cecchini et al., 2010). Even with salt intake level of less than 5g/person/day, as recommended by WHO, studies show that salt intake across many elite population groups in Africa is quite high at about 9-12g/person/day (Asaria et al., 2007). Due to effects of urbanization and gradual change to western diets, cholesterol and sugar intake have been on the increase in many African settings, especially among urban dwellers

(Cecchini et al., 2010). In addition, there is generally low consumption of fruits and vegetables in many African settings (Lim et al., 2012). Reports show that reduced fruits and vegetables consumption accounted for about 1.7 million deaths (16 million DALYs) globally in 2008, with Africa responsible for about a third of these deaths (World Health Organization, 2008).

Physical inactivity

Physical inactivity (or sedentary lifestyle) accounted for 3.2 million deaths globally (32.1 DALYs) and caused about 20-30% increase in NCDs mortality annually. Obesity and overweight are directly related to sedentary lifestyles, and have accounted for 2.8 million deaths globally (35.8 million DALYs) (Lim et al., 2012); this is highest in America and lowest in South-East Asia, while Africa falls between these regions (Lim et al., 2012).

Infections

Infections have been partially responsible for the high cancer burden in Africa (Martel et al., 2012). HIV/AIDS, Hepatitis B Virus (HBV), Human Papilloma Virus (HPV) and Helicobacter Pylori are the main causes (Sylla and Wild, 2011).

-*HIV/AIDS and NCDs*: The burden of HIV/AIDs in Africa may have also contributed to the growing burden of NCDs, as studies have shown that people with HIV/AIDS present with higher rates of NCDs compared with people who are HIV negative (Byass et al., 2013a). There are reports of direct biological linkages between HIV and some specific NCDs including Kaposi's sarcoma, HIV associated lymphoma, and cervical cancer; many of which are due to HIV opportunistic infections (UNAIDS, 2011). Other linkages have been thought to be as a result of the effects of HIV medications, treatment and the psychological state of the HIV patient (Oti, 2013). For example, in a study in Kenya, the prevalence rates of hypertension and obesity were significantly higher among HIV positives compared to those that were negative (UNAIDS, 2011). Some experts have reported that this may be due to lipodystrophy and metabolic consequences of some HIV treatments (Estrada et al., 2006). For example, according to Estrada and colleagues, in a 6-month study of 156 HIV patients on anti-retroviral treatment (ART) matched with 156 healthy controls,

the prevalence of lipodystrophy and metabolic syndrome was higher in HIV patients on ART than in the non-HIV infected healthy controls (15.8% vs 3.2%; P < .001) (Estrada et al., 2006). In addition, due to better health care, and with many HIV patients now relatively living longer, the prevalence of NCDs is also increasing among HIV positives, just as has been reported in the general population (UNAIDS, 2011). In a recent study in five African countries to examine the distribution of cause-specific mortality among HIV-negative and HIV-positive people using an InterVA-4 verbal autopsy interpretative model, Byass and colleagues reported that deaths from many NCDs were relatively higher among HIV positives compared to the negatives, with a mortality rate ratio for diabetes of 5.0, for stroke of 2.2, for COPD of 1.6, for asthma of 8.0 and for reproductive neoplasms of 14.3 (Byass et al., 2013a) (see **Table 1.3**). One promising thing from these apparent similarities is the fact that a lot can be learned in the response to NCDs from the current response to HIV/AIDS globally. Byass and colleagues noted the fact that many developing countries, especially in Africa, with a relatively higher burden of HIV, also have burgeoning epidemics from many NCDs (Oti, 2013). Specifically, many NCD patients and those living with HIV tend to present with few symptoms at the early stages of the respective diseases (Narayan et al., 2011). Additionally, both HIV/AIDS and NCD patients require regular hospital visits, follow-up investigations, adherence to medications, and adoption of healthy or safe lifestyles (Oti, 2013). Thus, HIV/AIDS and NCD control programmes may share similarities in the development of intervention models and tools and protocols (Oti, 2013). These may include: promoting healthy behaviours, long-term adherence to medications, monitoring of treatment outcomes, and involvement of patient and family in the final care pathway (Narayan et al., 2011). Further discussion on infections and NCDs is included in *Section 4.3.1*.

Table 1.3. Cause-specific mortality by HIV status using InterVA-4verbal autopsy interpretative model

WHO VA cause of death by InterVA-4	**Mortality rate HIV-*	**Mortality rate HIV+*	*Mortality rate ratio*
Oral neoplasms	0.01	0.14	19.2
Digestive neoplasms	0.06	0.76	13.0
Respiratory neoplasms	0.04	0.23	6.0
Breast neoplasms (female)	0.01	0.07	9.6
Reproductive neoplasms (female)	0.02	0.34	14.3
Other neoplasms	0.03	0.21	7.7
Diabetes mellitus	0.06	0.28	5.0
Stroke	0.07	0.15	2.2
COPD	0.04	0.07	1.6
Asthma	0.02	0.19	8.0
Other NCDs	0.04	0.17	4.6

**mortality rate per 1000 per year, VA-verbal autopsy*
Source: (Byass et al., 2013a)

Age, sex and race

Age, sex and race are non-modifiable risk factors for many NCDs. Prevalence of increased blood pressure is more common in Africa, among older age groups, and men (Edwards et al., 2000). Smoking and alcohol consumption in Africa is 6 times more prevalent among men, while obesity and sedentary lifestyle are common among women (Kengne et al., 2007, Msyamboza et al., 2011). Studies have also shown that Africa women have the highest risk of cervical cancers in the world (World Health Organization, 2011c).

Other factors

Many other risk factors of NCDs are associated with social determinants of health. A study in South Africa revealed that people may decide to change their eating patterns and physical activities due to socioeconomic and environmental influences (Stern et al., 2010). For example, a buzzing and busy urban life, which may be associated with night clubs, smoking and increased use of alcohol in many African cities, has been tagged socially informative, while weight gain and obesity, especially among African

women, are thought to be signs of healthy living and a good way to earn social respect (Stern et al., 2010).

As noted above, several studies have shown that poverty and lower living standards could be responsible for the increasing trend of NCDs in Africa and vice-versa (de-Graft Aikins et al., 2010b). The conclusions of some authors in South Africa suggested there could be other factors playing a role, too (Stern et al., 2010). For example, many behavioural risk factors of NCDs are common among people of lower socioeconomic status, or those who live in resource-poor settings. They often have a higher risk of dying from NCDs because they are constrained with worse access to health care, which is needed for timely diagnosis and treatment of NCDs, than the people in the higher socioeconomic status (Schneider et al., 2009, Di Cesare et al., 2013). On the contrary, the prevalence of overweight and obesity in many African settings has been reported to increase with rising levels of income due to more sedentary lifestyles and increased consumption of unhealthy diets (Dalal et al., 2011). Moreover, based on records in high income countries, many people are also obese and overweight, having varying degrees of NCDs as well (Di Cesare et al., 2013). Hence, NCDs burden is increasing in many African countries. This may not only be due to lower income statuses, but also several determinants of health may be responsible, including the lack of timely access to health care services (Dalal et al., 2011). The wealthy, therefore, are not immune to NCDs, but they may have the resources to manage them better if detected early enough (Di Cesare et al., 2013). Largely, the socio-economic impact of NCDs cuts across all ages, sexes, the poor and the rich.

1.1.6 Assessing the Gaps in Information, Control and Response to Non-Communicable Diseases in Africa

Gaps in information

The global target in 2005 was to reduce NCDs by 2% every year (World Health Organization, 2011a). Efforts toward achieving this goal have been delayed at various levels due to many reasons, some of which are yet to be fully identified (Asaria et al., 2007). Specifically, cost-effective, evidence-based and contextually feasible delivery strategies for NCDs programmes have been developed at country levels. However, the coverage of these interventions in Africa still remains low, especially due to poor health information management system, and a weak and fragile health system across many African countries (Kirigia and Barry, 2008). Recently, the world's health ministers agreed to work towards reducing premature mortality from the four main NCDs (cardiovascular diseases, diabetes, cancer and chronic respiratory diseases) by 25% from 2010 levels by 2025 (the "25 by 25 goal") (Beaglehole et al., 2013). It is important to further point out that "*premature*" in this context is defined as the probability of dying from NCDs between the ages of 30 years and 70 years (Kontis et al., 2014). Generally, the assumption before now is that NCDs predominantly affected the old. However, emerging data from Africa and many developing countries point to a significant amount of people aged between 15-59 years that are suffering from NCDs (Barry et al., 2009, Kengne and Mayosi, 2014). In 2008, about 44% of all NCD deaths occurred before the age of 70 globally (World Health Organization, 2008). Cardiovascular diseases accounted for 39%, followed by cancers at 27%, diabetes 4%, and chronic respiratory diseases, digestive diseases and other NCDs together accounted for about 30% of these deaths (World Health Organization, 2008). These deaths are avoidable and may not have occurred if timely and effective medical intervention had been made available (Kontis et al., 2014). In other words, significant proportions of deaths from NCDs in this age group may be indicative of failing national health systems, and this has apparently been the case in many African settings (Barry et al., 2009). With the recent goal of attaining a 25% global reduction in premature mortality from non-communicable diseases

(NCDs) by 2025 (the "25 by 25 goal"), experts have further stated there may be a need for health system strengthening, capacity building, and establishing rigorous data registration, collation and monitoring systems (Beaglehole et al., 2013).

Meanwhile, many African countries actually have a unit responsible for NCDs at national levels, but the effectiveness of those units remains a major source of concern, owing to the rising NCDs burden in the continent (World Health Organization, 2011c). In fact, in most African countries, the annual health expenditure on NCDs is relatively high, yet with very minimal impact (Asaria et al., 2007). This is basically due to misplaced priorities, administrative negligence, and technical incompetence, among many others (World Health Organization, 2011a). For example, Nigeria, Egypt and South Africa have structures in place for NCDs, including those for funding, health information and reporting system, and a variety of program specific policies and action plans, yet the burden of NCDs in these countries remains high (World Health Organization, 2011a).

Additionally, the lack of a national information system in many African countries has affected research output on NCDs in the continent (Gill et al., 2001). In the last two decades, there have been gradual increase in population-, hospital- and registry-based studies conducted across many parts of Africa, but the incompleteness of information from these studies have prevented further research from which inferences and policy decisions may be made (Opare et al., 2013). The few continent-wide estimates on NCDs are based on advanced statistical modelling, rather than the actual data on these diseases in Africa (Fan and Lam, 2012). Thus, the true representation of these estimates, with regard to the total African population, may still not yet be realised.

Gaps in Control

Tobacco and Alcohol Control: Moodie and colleagues expressed that transnational corporations have been the major drivers of NCDs in many African countries, and have greatly profited from increased consumption of tobacco and alcohol products in these countries (Moodie et al., 2013). Due to major roles played by these transnational corporations in Africa, they have been involved in decisions related to policies (Otañez et al., 2009). It has therefore been very difficult to fully implement tobacco and alcohol control measures, as this may directly affect their sales (Moodie et al., 2013). Research findings have shown that tobacco control has been proven to be cost-effective in reducing NCDs compared to many other interventions globally (Adejuwon, 2009, Amuyunzu-Nyamongo, 2010). For example, Egypt increased taxes on tobacco by 87%, Turkey 77% and Ukraine 127%; and between 2009 to 2010, Turkey was considered one of the 17 world's smoke-free countries, while Egypt and Ukraine experienced drastic reductions in tobacco consumption and consequently NCDs (World Health Organization, 2011a). In addition, implementing four key elements of WHO 2006-2015 Framework Convention on Tobacco Control (FCTC), which would amount to about $0.4-1.0 per person per year in Africa, has been adjudged a major and affordable contribution towards the reduction of NCDs in the continent (Asaria et al., 2007). Moreover, increased taxes, regulatory sanctions, drink driving control measures are also cost effective interventions for reducing harmful alcohol use (World Health Organization, 2011b). While some studies showed varying levels of drink driving control measures in Africa, the systems in these countries are not well equipped to fully implement this (Amuyunzu-Nyamongo, 2010).

Salt, Cholesterol and Fats Control: Salt reducing policy is currently in use in the UK and has been very cost-effective (Asaria et al., 2007). The programme began in 2003 and by 2008, average daily salt consumption per person had reduced from 9.5g to 8.6g, averting over 6000 deaths. In addition, more than £1.5 million per year was saved (World Health Organization, 2011a). According to Asaria and colleagues, 13.8 million deaths could be averted with a 15% individual reduction in salt intake (Asaria

et al., 2007). In Africa, reports reveal that many countries are yet to adopt this policy (Asaria et al., 2007). Meanwhile, the growth of processed foods and fast-foods restaurants is on the high in many African settings, and there are not yet effective measures to monitor the content of their products (Amuyunzu-Nyamongo, 2010). In fact, just like the tobacco and alcohol companies, influential processed foods companies are also employing similar strategies to undermine the implementation of healthy public polices for NCDs in Africa (Otañez et al., 2009, Moodie et al., 2013). According to experts, there should be no place for any unhealthy commodity industries in the formation of national or global policy for non-communicable diseases (Moodie et al., 2013, Bonita et al., 2013). The Disease Control Priority Project (DCPP) highlighted that ensuring only poly-unsaturated fatty acids in processed foods could avert one DALY from NCDs at a cost of $4012 in North Africa (World Health Organization, 2011a, DCPP, 2011).

> "The most sustainable method for raising additional revenue for NCD prevention and management is to develop a health promotion fund (or the equivalent) by substantially and regularly increasing the price of tobacco, alcohol, and unhealthy food products through large and phased increases in taxes". Robert Beaglehole (Beaglehole et al., 2013)

Gaps in response

Access to essential medicines, vaccines and screening tools: According to Hogerzeil and colleagues, access to essential medicines and vaccines specific for the treatment of NCDs is unacceptably low globally (Hogerzeil et al., 2013). Hepatitis B Virus (HBV) and Human Papilloma Virus (HPV) vaccination, and routine screening for cancers, have been found to be cost-effective in addressing the increasing incidence of cancers (Sylla and Wild, 2011). However, due to the huge capital involved and failure to get willing international partners, many African countries have been unable to fully implement this (Amuyunzu-Nyamongo, 2010). Experts have advised that with an appropriate use of generic medicines coupled with efficient selection and procurement process, more medicines may be acquired within existing budget in Africa and many LMIC globally (Hogerzeil et al., 2013). Importantly, the success of existing drug initiatives in the treatment of HIV in Africa may offer valuable lessons that can promote access to pharmacological management of NCDs in the continent (Hogerzeil et al., 2013)**.**

Monitoring, Surveillance and Research: A NCDs surveillance framework has been developed by the WHO, and this involves monitoring the exposures (risk factors), outcomes (NCD cases and fatalities) and responses (health system capacity) towards developing a sustainable policy for the control, prevention and management of NCDs (World Health Organization, 2011a, Alwan et al., 2010). Records show that this is clearly lacking in many African countries, as they lack efficient data collation and registration system (Msyamboza et al., 2011, Unwin et al., 2001). Poor research output is another major challenge that has ensued from the lack of data (Dalal et al., 2011). African governments have been tasked with the responsibility of prioritizing cancer prevention through regular and up to date cancer registration system, support and research training for people working in cancer control centres (Sylla and Wild, 2011). Research focussing on estimation of the burden of NCDs, risk factors, and re-organizing the health system or primary healthcare services towards providing an effective response to the challenges posed by NCDs could be productive (McCarthy et al., 2010, Maher et al., 2010).

Health system strengthening and capacity building: This involves a system aimed at improving health care (service delivery), physical (infrastructural), financial (funding), and human (health workforce) sectors respectively (World Health Organization, 2011a, Alwan et al., 2010). It cuts across many other areas of health system development, and may require skilled experts and efficient human resource personnel (Samb et al., 2010). With the current weak health systems in many African countries, coupled with poor funding and organization, capacity building and service delivery have been remarkably low (Samb et al., 2010).

Poverty and hunger: Research findings have shown that socio-economic status and many other determinants of health like poverty, hunger, uneven wealth distribution and illiteracy contribute to the growing burden of NCDs across many settings, especially in Africa (Schneider et al., 2009). The World Bank estimated that about one-third of the poorest two quintiles in Africa and many developing countries die prematurely from NCDs (World Bank, 2014a). Since this disproportionately affects the most economically productive age groups, families are further thrown into a chronic poverty trap (Schneider et al., 2009). According to researchers, about 44% of the African population are under 15 years of age, and the transition to adulthood in a predominantly poor setting may have contributed to the high prevalence of NCDs (Bradshaw and Steyn, 2001). A study reported that as children grow older they carry along risks accumulated from sub-standard living conditions, unhealthy and risky behaviours, and metabolic consequences of poor feeding and under-nutrition in childhood (Stanciole et al., 2012). By middle-age, body systems may not be able to respond well to these lifestyles. This group of children may consequently become a sick generation with a likely early onset of diabetes, stroke, cancer and other chronic diseases (Bradshaw and Steyn, 2001). As noted earlier, a complex host of risk factors may be attributed to the development of NCDs in a population, some of which have been considered under *risk factors* and *heterogeneities within and between African population groups*. Therefore, it is important to note that continuing hunger and poverty to adulthood may only be contributory to this complex risk factors pattern. There are indeed other factors that may be considered, including those related to the fetal origins of adult disease (FOAD) (Skogen and Øverland, 2012). The FOAD

hypothesis suggests that the risks from intrauterine environmental exposures may affect the development of the fetus during sensitive fetal growth periods, and may consequently increase the risk of some diseases in adulthood (Barker, 1992). According to Barker, this relationship was first observed between some intrauterine exposures and the development of adult coronary heart disease (Barker, 1992); however, further studies have showed a range of links with some other chronic diseases (Skogen and Øverland, 2012). Although some researchers have stated that the relationship between intrauterine life and adult diseases remain unclear and perhaps independent (Ben-Shlomo and Kuh, 2002), other experts have supported this hypothesis, while showing further evidence that environmental exposure during pregnancy can actually have effects on an individual's health during adult life (Whincup et al., 2008, Alati et al., 2007).

Meanwhile, with largely weak health systems across many African settings, any co-ordinated public health response (if at all present) may be further overwhelmed, and many affected individuals may still lack the financial strength to seek appropriate medical attention (Schneider et al., 2009). One other factor that has been reported is that problems and ill-effects of NCDs in Africa and other poor settings far outweigh what is experienced in high income countries, and this possibly points to an intrinsic relationship with poor living conditions (World Health Organization, 2009). For example, age-standardized NCDs mortality rates have been reported to be highest in Africa in 2008, and are rising faster than in other world regions (World Health Organization, 2011a). Many poor and rural populations with NCDs are doubly disadvantaged in terms of access to health services (World Health Organization, 2009). A study in Tanzania reported that Tanzanian men aged 15-64 years were three to six times more likely to die from stroke compared to those in the United Kingdom (Walker et al., 2000). There are also emerging reports that the percentage of daily smokers is higher in poorest countries, including those in Africa, compared to high income countries (Jha et al., 2002). As noted earlier, a major factor here may the lack of effective government action in these settings to institute appropriate counter smoking legislation (Adejuwon, 2009). According to WHO, NCDs may still lead to a further poverty trap, as 2-3% of people in low-income settings are faced with

catastrophic health expenditure from NCDs, and this pushes about 1-2% into further impoverishment (World Health Organization, 2009). Thus, many have reported that efforts towards achieving MDG-1 (eradicate extreme poverty and hunger) could help address many NCDs and in return further strengthen the achievement of this goal.

However, while poverty and hunger may be associated with NCDs, it is also worthwhile to state that wealthy lifestyles and affluence may also be associated with major behavioural risk factors of NCDs, including unhealthy diet, sedentary lifestyles and obesity. Reports show that about 60-80% of NCDs in the developing world occur due to these behavioural lifestyles (Schneider et al., 2009). Obesity is currently described as a global pandemic affecting about 500 million people worldwide, while physical inactivity is said to have resulted in annual deaths almost equal in number to those caused by tobacco smoking (World Health Organization, 2009). In urban South Africa, over 50% of adult women and 30% of adult men in the middle to upper socio-economic class are either obese or overweight (Bradshaw and Steyn, 2001). Many of these sit long hours at work every day, eat from fast food restaurants (with high fat and salt content food), drive in private luxurious cars, and engage in very limited physical activity (Lambert and Kolbe-Alexander, 2013). This shows that beyond poverty and hunger, wealth and affluence are also important drivers of the NCDs pandemic. In fact, the pandemic of NCDs may be described as a product of a poorly managed development process, unhealthy industrialization and adoption of western lifestyles, all in the presence of a health system that is unaffordable, unavailable and insensitive to the health needs of those who require it most (Bradshaw and Steyn, 2001, Schneider et al., 2009). Therefore, population-wide measures targeting poverty and hunger may need to be implemented with caution. There is need for a holistic approach in the fight against NCDs in Africa, while carefully considering all possible contributory factors (Dalal et al., 2011, Schneider et al., 2009). Most African governments still do not have these encompassing population-wide interventions (Schneider et al., 2009).

Table 1.4. The six objectives of the 2008-2013 action plan on NCDs

#	***Objectives***
1	To raise the priority accorded to non-communicable disease in development work at global and national levels, and to integrate prevention and control of such diseases into policies across all government departments
2	To establish and strengthen national policies and plans for the prevention and control of non-communicable diseases
3	To promote interventions to reduce the main shared modifiable risk factors for non-communicable diseases: tobacco use, unhealthy diets, physical inactivity and harmful use of alcohol
4	To promote research for the prevention and control of non-communicable diseases
5	To promote partnerships for the prevention and control of non-communicable diseases
6	To monitor non-communicable diseases and their determinants and evaluate progress at the national, regional and global levels

Source: WHO 2008-2013 Action Plan (World Health Organization., 2007)

One vital response to the growing epidemics of NCDs globally, with particular focus on Africa, is the WHO 2008-2013 action plan for the global strategy for the prevention and control of non-communicable diseases (World Health Organization., 2007), which basically had six objectives targeted at addressing the burden of NCDs at various levels (**Table 1.4**). Emerging research findings have further shown that these interventions can address many NCDs risk factors in Africa, only if relevant resources can be harnessed towards implementing this (McCarthy et al., 2010, Samb et al., 2010). Bonita and colleagues further stated that strong leadership from country heads of state and governments, cutting across the basic key steps of planning, implementation, and accountability, is essential (Bonita et al., 2013).

1.1.7 Specific NCDs reviewed in this thesis and reasons for this choice

In this thesis, the specific NCDs reviewed are:

i. Cardiovascular diseases (mainly *hypertension* and *stroke*)

ii. Diabetes mellitus

iii. Cancer (mainly *cervical, breast, prostate, ovary, oesophagus, bladder, Kaposi, liver, stomach, colorectal, lung* and *non-Hodgkin lymphoma*)

iv. Chronic respiratory diseases (mainly *COPD* and *asthma*)

According to the WHO global burden of disease (GBD) report, these four NCDs were estimated to be the leading causes of deaths globally, accounting for about 80% of global deaths from all NCDs. As noted earlier, cardiovascular diseases (CVDs) ranked highest, accounting for 17 million deaths (48% of global NCDs deaths) (World Health Organization, 2008). Cancer accounted for 7.6 million deaths (21% of global NCDs deaths), chronic respiratory diseases (CRDs) 4.2 million deaths (11.7% of global NCDs deaths) and diabetes 1.3 million deaths (3.5% of global NCDs deaths) (**Table 1.1**) (World Health Organization, 2008).

In Africa, the pattern appears to be largely the same as that observed globally. Cardiovascular diseases accounted for 10% of all deaths in the African region, cancer accounted for 4%, CRDs 3%, and diabetes 1% (World Health Organization, 2014b). These translated into about 1.3 million deaths from CVDs in Africa (3.5% of global NCDs deaths), followed by cancer, accounting for 0.4 million deaths (1.1% of global NCDs deaths), CRDs, for 0.3 million deaths (0.9% of global NCDs deaths), and diabetes, for 0.2 million deaths (0.5% of global NCDs deaths) (World Health Organization, 2008), see **Table 1.1**.

For cardiovascular diseases, the leading causes of deaths include stroke, ischemic heart disease and hypertensive heart disease (World Health Organization, 2008). From an initial scoping review conducted on Africa, there was very scanty literature on ischemic heart disease and hypertensive heart disease. Thus, the main CVD included in the early phase of writing this thesis was stroke. However, further

literature review revealed a high number of published papers on hypertension. As this is a leading risk factor for most CVDs, this was also included in the thesis. Thus, the reviewed CVDs in this thesis were *hypertension* and *stroke*.

For the choice of cancer types reviewed, this was also based on global and regional estimates for Africa, respectively. According to GLOBOCAN, the top five cancers worldwide in 2008 were lung, breast, colorectal, stomach, and liver cancer. Parkin and colleagues in a separate review for Africa reported that the top six cancers in Africa among women were *cervical cancer, breast cancer, Kaposi's sarcoma, liver cancer, non-Hodgkin lymphoma (NHL)* and *ovarian cance*r, and among men, these were *Kaposi's sarcoma, liver cancer, prostate cancer, bladder cancer, NHL* and *oesophageal cancer* (Parkin et al., 2008). Therefore, in an attempt to have a better epidemiological knowledge of cancer types in Africa and to allow for relevant global comparisons, I limited my review to these top causes of cancer. Data on cancer that were extracted and analysed therefore included the top six cancers in Africa in both sexes (listed above), in addition to *lung*, *colorectal*, and *stomach* cancers, which were the most important cancers globally (that were not listed in Africa by Parkin and colleagues) (Parkin et al., 2008). Therefore, the final cancer types reviewed were 12 in all: *cervical, breast, prostate, ovary, oesophagus, bladder, Kaposi, liver, stomach, colorectal, lung* and *non-Hodgkin lymphoma*.

According to the WHO GBD report, about 300 million people have asthma, and 210 million people have COPD (World Health Organization, 2008). The WHO also estimates that COPD is responsible for about 3 million deaths globally in 2011 (4^{th} leading cause of deaths), accounting for about 9.1% of all NCDs deaths (World Health Organization, 2011a). Meanwhile, with an estimated 300 million people living with asthma, and current trends also suggesting that an additional 100 million people may be living with asthma by 2025; asthma has been rated the most common chronic disease affecting children (IUATLD, 2011). The World Health Organization (WHO) estimated about 250,000 deaths from asthma annually, mostly in low- and middle-income countries (LMIC) (Bousquet et al., 2010, Braman, 2006). With these two (*COPD* and *asthma*) being the top CRDs globally, they therefore were the main CRDs reviewed in this thesis.

Each of these four NCDs under review will be briefly examined in the next four sub-sections.

1.1.8 Cardiovascular Diseases

Cardiovascular diseases rank among the leading causes of disabilities and deaths from non-communicable diseases (NCDs) in Africa (Lawes et al., 2006, World Health Organization, 2013b), with rising prevalence and death rates now observed more in young and active adults (Opie and Seedat, 2005). Recently, the African Union (AU) reported that cardiovascular diseases are one of the greatest health challenges after HIV/AIDS in the continent (WHO Regional Office for Africa, 2006). This is in fact a priority globally as conclusions from the 2011 United Nations high level meeting on NCDs focus on a reduction of hypertension and other CVDs, especially in Africa, where the burden is rising at a faster rate compared to other parts of the world (Beaglehole et al., 2011). Worldwide, cardiovascular diseases account for about 17 million deaths, with complications from poorly controlled hypertension resulting in over 7.5 million deaths and 57 million disability adjusted life years (DALYs) (Kearney et al., 2005).

Hypertension

The relatively higher prevalence of hypertension in Africa has been linked to population growth and ageing, rising urbanization, mass migration from rural to urban areas, and an increased uptake of western lifestyles including tobacco and alcohol consumption (Opie and Seedat, 2005, de-Graft Aikins et al., 2010b). Public health response from the governments of many African nations still remains low, as research findings show that a high number of hypertensive individuals are currently unaware of their condition (Kayima et al., 2013). Many African countries are yet to implement high blood pressure awareness and control programmes on a population-wide scale, even to people with very high risk of cardiovascular complications (MacMahon et al., 2008). Even with a widely popularised availability of hypertension treatments in some African countries (Mohan et al., 2013), reports show that many rural dwellers are still faced with lack of antihypertensive medications and poor management of cases of hypertension (Perkovic et al., 2007). The WHO has recommended a need for strong public health policies, multisectoral approach, and available and affordable treatment options toward reducing this growing burden of hypertension in Africa (World Health Organization, 2013b).

Despite reports of a higher prevalence of hypertension in Africa compared to other world regions (World Health Organization, 2013b), public health experts believe the real burden is still far from being known (Addo et al., 2007). Many studies in the 1980s and early 1990s were based on the old definition of hypertension (≥ 160/95 mm Hg) (Kayima et al., 2013, Addo et al., 2007). These surveys may possibly underestimate the prevalence of hypertension in Africa in comparison to newer surveys based on ≥ 140/90 mm Hg cut off level. Moreover, even within studies based on similar case definitions, the variation in reported estimates still suggests the need for more systematic and accurate estimates from larger number of studies towards appropriately informing health service planning and a better response to hypertension in Africa. For example, the WHO reported that the prevalence of hypertension in the African region was highest globally in 2008, with an estimated prevalence of 46% (World Health Organization, 2011a). This, though vital for instituting relevant public

health response in the continent, elucidates a conflicting state of data in comparison to other hypertension prevalence estimates in Africa which are relatively low (Kengne et al., 2012, Twagirumukiza et al., 2011). Thus, with an increased research output on hypertension in Africa in the last two decades, it is important to conduct systematic review of population-based studies towards providing an improved continent-wide estimate of the prevalence and awareness of the rate of hypertension in Africa, which hopefully may encourage healthy public health policy for a value-added management of hypertension in the region.

Stroke

The burden of stroke is increasing in many low- and middle-income countries (LMIC) (Feigin et al., 2014), and due to high fatality rates and overwhelming resource incurred by the health systems, stroke and many non-communicable diseases (NCDs) are now targeted public health priorities in these regions (Beaglehole et al., 2011, Chin, 2012). Global estimates suggest about 16 million new cases of stroke and 62 million stroke survivors in 2005, with deaths from stroke accounting for 9.7% of all global deaths (World Health Organization, 2011a). In the absence of significant global public health response, this is expected to increase to over 23 million new stroke cases and 7.8 million stroke deaths by 2030 (Strong et al., 2007, World Health Organization, 2004).

It has been estimated that LMIC account for over 87% disability adjusted life years (DALYs) from stroke, which is about seven times the DALYs lost in high-income countries (HIC) (Johnston et al., 2009). Africa is particularly worst hit, owing to population growth, unchecked industrialization and increased consumption of western diets. This is due to a rise in many modifiable vascular disease risk factors including smoking, harmful use of alcohol, physical inactivity and unhealthy diets, and invariably resulting in increased prevalence of hypertension, diabetes and obesity (Connor et al., 2007, O'Donnell et al., 2010). In 2000, two African countries, although recorded low stroke prevalence rates, had remarkably high stroke incidence rates (Truelsen et al., 2006). According to GBD 2002 estimates, three African countries (Angola, Liberia and Sierra Leone) recorded the highest stroke mortalities and DALYs worldwide (World Health Organization, 2002, World Health Organization, 2004). Between 2002 and 2004, estimates further revealed an increasing prevalence with 8% of new stroke cases and 5% of stroke survivors occurring in Africa (Truelsen, 2010a). In 2004, stroke was estimated to cause over 3% of all deaths in the African region and about 52% of all CVD deaths (Connor et al., 2007). Even with this increasing burden, the public health response, accesses to health services and treatment options in many African countries have been poor (Wahab, 2008, Connor et al., 2007). Specifically, the lack of functional stroke units,

neurologists, health workers, cranial computed tomography (CT) scans, magnetic resonance imaging (MRI) machines and echo-doppler machines, among many others, has negatively affected stroke outcomes (Wahab, 2008, Chin, 2012). Moreover, the high cost of medical care in a relatively low-income African society could have resulted in high stroke fatalities, as some studies have indicated that stroke prevalence and deaths in Africa increased due to an overtly poor socioeconomic status (Johnston et al., 2009). For example, a recent study revealed the incidence of stroke in HIC decreased by over 40% between 1970 and 2008, but with actual number of stroke cases increasing due to ageing of the population (Feigin et al., 2009), while in Africa and many LMIC, stroke incidence rose by over 100% over the same period (Feigin et al., 2009). Furthermore, due to the high proportion of undiagnosed hypertension in Africa, especially among the younger population (Mensah, 2008), stroke incidence has also been reported to be more severe and higher among the active and productive population age groups (Walker, 1994).

Meanwhile, the World Health Organization (WHO) technically supported member countries with methods for improved data collation and registration of hospital stroke cases (Mathers, 2005). Notwithstanding, another set-back in the response to the management of stroke in Africa is the lack of data and low research output (Mensah, 2008, Connor et al., 2007). Stroke case ascertainment and survey methodologies have not, in most cases, complied with international protocols (Connor et al., 2007). Published research studies are characterized by poorly organized community-based studies, difficulties in making retrospective diagnosis, and overlapping cases of first and recurrent strokes (Sudlow and Warlow, 1996, Connor et al., 2007). The few studies on stroke, therefore, could have been marked by under-estimation of the stroke burden in Africa. In view of this high burden of stroke, its public health importance, and the relatively low research output in Africa, it is important to estimate the incidence and prevalence rates of stroke in Africa in order to attempt to quantify the burden and inform decision regarding policy responses and health system interventions across many countries in the region.

1.1.9 Diabetes

Diabetes and other non-communicable diseases (NCDs) have been on the increase over the last three decades in Africa, posing huge burden on the economy of the continent (Kirigia et al., 2009), especially with a competing need for health resources from many infectious diseases (Barry et al., 2009, Beaglehole, 2011). Diabetes has been regarded as a disease of the affluent, and thought to be rare in Africa (Skene et al., 1982); however, recent reports show that diabetes is now prevalent and by 2030, NCDs, including diabetes and hypertension, will be among the leading causes of deaths in Africa (Murray and Lopez, 1996). Many research findings have shown that diabetes prevalence estimates in urban Africa are similar with, or even higher than, what is obtained in developed countries (Beran and Yudkin, 2006); this downplays previous reports of lower prevalence of diabetes in Africa (Skene et al., 1982). Experts still report that despite a relative increase in diabetes research in Africa, there still not enough epidemiological evidence to estimate the prevalence of diabetes in the region; most estimates have been based on sophisticated modelling, and may not necessarily reflect the true burden of the disease (World Health Organization, 2006).

According to International Diabetes Federation (IDF) atlas, about 151 million people were estimated to have diabetes globally in 2000 (International Diabetes Federation, 2000), 194 million in 2003 (International Diabetes Federation, 2003), 246 million in 2006 (International Diabetes Federation, 2006), 285 million in 2010 and a projected increase to 439 million in 2030 (Walker et al., 2011, International Diabetes Federation, 2009), which is an increase of 54% from the 2010 figures. This global increase was also documented in Africa; this has been linked with the fast demographic changes, uncontrolled urbanization and the gradual adoption of western lifestyle (Mbanya et al., 2010). Wild and colleagues estimated 7.1 million diabetic cases in Africa in 2000, and a projected increase to 18.6 million in 2030 (161% increase) (Wild et al., 2004). IDF also reported about 10.8 million diabetic cases in 2006 (International Diabetes Federation, 2006), 12.1 million in 2010 and a projected estimate of 18.7 million in 2025, and 23.7 million in 2030 (International Diabetes Federation, 2009, Shaw et al., 2010), giving about 98% increase between 2010 and

2030, doubling the estimated global increase. Mbanya et al. also reported that diabetes prevalence is increasing in sub-Saharan Africa, with a regional prevalence of 2-3% in mid-1990s increasing to about 4.6% in 2010 (Mbanya et al., 2010). Based on IDF estimates, the top 5 countries with highest diabetes population in Africa in 2000 were Nigeria (1.71 million), South Africa (0.81 million), Ethiopia (0.79 million), Algeria (0.43 million) and Ghana (0.30 million) (International Diabetes Federation, 2000).

As noted earlier, the high burden of HIV/AIDS has relatively affected the occurrence of many NCDs, including diabetes, in Africa, with a reported similar trend in the mortality rate of diabetes and HIV/AIDS in the region (Kalk and Joffe, 2008, Levitt and Bradshaw, 2006). In fact, emerging evidence in western and eastern parts of Africa points to a stable or diminishing spread of HIV/AIDS, it may therefore be assumed that the burden of diabetes is also decreasing. However, comparative models in Southern Africa, where HIV/AIDS burden is highest in Africa, have shown an increasing prevalence of diabetes mainly due to population changes and increased life expectancies, irrespective of the impact of HIV/AIDS (Levitt and Bradshaw, 2006, Panz and Joffe, 1999). Based on the recent GBD estimates however, deaths from diabetes globally increased from 16.3/100000 to 19.5/100000, and DALYs also increased from 523/100000 to 680/100000 between 1990 and 2010, respectively (Lozano et al., 2012, Murray et al., 2012). In Africa, however, there have not been many studies on diabetes mortality (Mbanya et al., 2006); the few reports have shown that the main causes of deaths are from complications and overriding infections (Mbanya and Ramiaya, 2006). The health cost from diabetes in Africa has also been huge (Mbanya and Mbanya, 2003, Chale et al., 1992); Kirigia and colleagues estimated that the 7.1 million cases of diabetes reported in Africa in 2000 accounted for a regional economic loss of about 25.5 billion US dollars ($), equivalent to about $3633 per diabetic case (Kirigia et al., 2009). The need for insulin and other medications was responsible for the bulk of the direct cost, accounting for about $8.1 billion ($1154/diabetic case) (Kirigia et al., 2009, Mbanya and Mbanya, 2003). Indirect cost was higher, with permanent disability from diabetic

complications largely indicated, accounting for about $17.4 billion (Kirigia et al., 2009).

From available evidence in Africa, Type 1 diabetes prevalence appears to be rarer, though experts still call for more studies involving larger population to validate this (Mbanya et al., 1997). In 1992, Nigeria reported prevalence of 0.33/1000 (Afoke et al., 1992), and in a 1989 survey of school children (aged 7-11 years) in Sudan, the prevalence was 0.95/1000 (Elamin et al., 1989). Tanzania had a low incidence of 1.5/100000/year in 1993 (Swai et al., 1993), while Elamin and colleagues reported incidence of 10.1/100000/year in Sudan in 1997 (Elamin et al., 1997). The huge contrast is believed to be due to ethnic differences and study designs, as the Tanzanian population were mainly indigenous Africans, while the Sudanese study had a mixture of Arab and African populations (Mbanya et al., 2010, Mbanya and Ramiaya, 2006). The age of onset of type 1 diabetes is quite later than what is obtained in developed countries (Beran and Yudkin, 2006). From studies conducted in Tanzania, South Africa and Ethiopia, the peak age at onset ranges between 22-29 years (Mbanya et al., 2006). There is still little evidence on the sex preference of type 1, though a female preponderance was reported in South Africa (Levitt, 2008).

As reported in many parts of the world, type 2 is the most common diabetes type in Africa (Levitt, 2008, Mbanya et al., 2010, World Health Organization, 2006), and prevalence now appears to be approaching what is obtained in western Europe (Levitt, 2008). Mbanya and Ramiaya reported that prevalence of type 2 diabetes was below 1% in most parts of Africa between 1960 and 1980, excluding Cote d'Ivoire (5.7%) and South Africa (0.6-3.6%) (Mbanya and Ramiaya, 2006). In 1990, type 2 cases reached about 3 million (King and Rewers, 1993), and projected to experience a 2-3 fold increase by 2010 (Wild et al., 2004). The prevalence of type 2 diabetes was highest among populations of Indian origins in South Africa and Tanzania, ranging between 12-15% in 1991 (Mbanya et al., 2010, Levitt, 2008). Generally, as of year 2000, type 2 prevalence ranged between 1% and 6% in most parts of Africa (Shaw et al., 2010).

Gestational diabetes has not been documented much in Africa. It is believed that about 7% of all pregnancies in Africa may be complicated by hyperglycemic episodes (Jiwani et al., 2012, Mamabolo et al., 2007). Impaired Glucose Tolerance (IGT) and Impaired Fasting Glycemia (IFG) prevalence varies across various age groups in most parts of Africa; rates between 5% and 10% are quite common, with IGT affecting more women than men, and IFG vice-versa (World Health Organization, 2006). Reports show that regions with relatively low diabetes prevalence but with fairly high prevalence of IGT and IFG may be at an early phase of diabetes epidemic (Mbanya et al., 2006). This was observed in Cameroon and Tanzania, both having low diabetes prevalence and raised IGT, and reportedly having high endemicity index of 83% and 88.4% respectively (Mbanya et al., 1997, McLarty et al., 1989). In an 11-year follow-up study of IGT cases in Mauritius, 30% returned back to normal blood glucose values, 35% still had IGT, 5% developed IFG and 5% developed diabetes; while in a similar follow-up of IFG cases, 40% reverted back to normal, 15% remained as IFG, 20% developed IGT and 25% eventually developed diabetes (Soderberg et al.).

Research findings have shown that complications from diabetes are high in Africa (Mbanya and Sobngwi, 2003). Acute complications of diabetes, mainly diabetic ketoacidosis (DKA), hyperosmolar non-ketotic coma (HONC) and hypoglycaemia, are frequent causes of hospital emergencies with high mortalities (Idemyor, 2010). In Tanzania and Kenya, DKA accounted for 25% and 33% diabetic emergencies respectively, with most cases presenting due to lack of insulin (Levitt, 2008). HONC is a common complication of type 2 diabetes, occurring due to combined effects from the lack of insulin, infection, and non-compliance with medications or diet; it accounts for about 10% of diabetic emergencies in Africa and other developing countries (Mbanya and Mbanya, 2003). Hypoglycemia occurs less frequently, with missed meals and inappropriate medications accounting for the observed cases (Levitt, 2008). Africa has high prevalence of chronic diabetic complications; retinopathy accounts for about 13%-55% of chronic complications, nephropathy 32%-57%, and foot ulceration 12%-20% (Mbanya and Ramiaya, 2006). Cardiovascular diseases may also complicate diabetes, commonly due to co-existing

hypertension (Mbanya et al., 2006); in an African study, about 15% of stroke patients were known diabetics (Aspray and Unwin, 2001).

Age and ethnicity are non-modifiable risk factors of diabetes. Diabetes increases with age, with peak age in Africa occurring in the age groups 20-44 years and 45-64 years (Aspray and Unwin, 2001, Mbanya et al., 2010). Indigenous Africans present with lower prevalence of diabetes than Africans living abroad; this also reflects influence of environmental factors (Swai et al., 1990). A comparative study showed higher diabetes prevalence among African populations in the Caribbean, United Kingdom and United States, compared with indigenous African populations in Western Africa (McLarty et al., 1990b, Palmer et al., 2012). As noted, environment factors have been associated with diabetes, especially in Western Europe, where seasonal viral infections reportedly led to increased incidence of hyperglycemic episodes (World Health Organization, 2006). In Africa, McLarty et al. reported seasonality of type 1 diabetes in Tanzania in 1989 (McLarty et al., 1989).

Family history of diabetes, including genetic and immunological predisposition, is another risk factor. Many type 2 diabetic cases discovered across various studies in Cameroon, South Africa, Nigeria, and Tanzania had about 5-10% positive family history of diabetes (Mbanya et al., 2010), with evidence suggesting linkage in four regions on chromosome 12, 19 and 20 (Rotimi et al., 2004). Type 1 diabetes in Africa is associated with human leucocyte antigens (HLA) DR3 and DR4, and also linked positively in some African populations with alleles DQB*0201/0302 and DRB*0301/0401, and negatively with DQB*0501 (Mbanya et al., 2001). Type 1 diabetes mainly results from islet cells auto-antibodies (McLarty et al., 1990a); however, across many studies in Tanzania, Nigeria, South Africa, and Ethiopia, type 1 diabetes also had immunologic links with glutamic acid decarboxylase and insulinoma associated protein-2 antibodies (McLarty et al., 1990a, Lutale et al., 2007, Panz et al., 2000). According to IDF, sex distribution of diabetes varies widely in Africa, with no specific trend (Shaw et al., 2010).

As indicated, rapid urbanization has been suggested as a major reason for increased prevalence of diabetes and other NCDs in Africa, as people tend to gradually adopt

western lifestyles including reduced physical activity, increased fats consumption, tobacco and alcohol consumption (Mbanya et al., 2010, Levitt, 2008). Improved standards of living also tends to make people take better medical care, with consequent increased life expectancies, change in population structure and increased prevalence of NCDs (McLarty et al., 1990b). Worldwide, Africa is experiencing fastest rate of urbanization, with over a third of the population currently residing in urban areas; this is expected to increase to about 45% by 2025 (World Bank, 1993, United Nations, 2012). It is believed that increased physical activity, usually from farming and walking, contributed to low prevalence of diabetes and hypertension in many rural African populations (Abubakari and Bhopal, 2008, Abubakari et al., 2009).

Increased adiposity, measured from body mass index (BMI), waist-hip circumference (WHC) or waist-hip ratio (WHR), is also a known diabetes risk factor in Africa (Abubakari and Bhopal, 2008). In South Africa, many studies reported high rates of obesity among diabetic patients, ranging between 58% and 65% (Levitt, 2008). Increased physical inactivity, high fat diets and urban environments may indirectly contribute to increased adiposity among Africans (Abubakari and Bhopal, 2008). Cultural beliefs and traditional norms have also contributed to increased burden of diabetes in Africa (Beran and Yudkin, 2006). The knowledge, attitude and perception on diabetes have been poor; people still alternate between modern and traditional medications, with this negatively affecting diabetes control and prevention programmes (Levitt, 2008).

As highlighted earlier, economic burden from diabetes has been really high; there is still the need for more research on economic cost of diabetes and other NCDs (Bloom et al., 2011). In a survey of 46 African countries in 2009, direct cost of diabetes care per individuals was about 25% of gross national income (GNI) per head for the 12 wealthiest countries, and a massive 125% of GNI per head for the remaining 34 poorest countries (Kirigia et al., 2009). According to the survey, diabetes presents huge financial burden on individuals, the society and government.

South Africa, Kenya, Zimbabwe, Nigeria and Ghana top the list of African countries spending hugely on diabetes in Africa (Walker et al., 2011).

Meanwhile, public health experts believe information on diabetes epidemiology over the last 10 years has increased in Africa, but is still limited in many areas (Unwin et al., 2010). WHO reports there is still a need for more research on the burden of diabetes, including country specific response to diabetes treatment and management, and anthropological and cultural perspectives of diabetes in Africa (World Health Organization, 2006). With a growing epidemic of diabetes in Africa, and many of these research gaps remaining unaddressed (World Health Organization., 2007), this study thus aims to estimate the prevalence of diabetes in Africa towards giving appropriate policy recommendations that can improve overall management of diabetes in the continent.

1.1.10 Cancer

The burden of cancer is increasing worldwide and currently a major contributor to global morbidities and mortalities (Arbyn et al., 2011). Cancer was previously thought to be a disease of the industrialized nations (Arbyn et al., 2011, World Health Organization, 2013a), however, evidence now shows that most new cases of cancers are found in low- and middle-income countries (LMIC), increasing from 15% in 1970, to 56% in 2008, and projected to reach about 70% by 2030 (Farmer et al., 2010). One major challenge is in the overall response to this growing burden in many LMIC, with poor health system response and consequently, low survival rates reported in many LMIC, compared to an improved response and survival rates in the developed countries (Coleman et al., 2008). In fact, due to rapid population growth, increasing life expectancy, and progressively westernized lifestyles in developing countries, and coupled with overall population ageing globally, the burden of cancer is expected to continue to rise (Parkin et al., 2003), with about 27 million incident cases, 17 million deaths, and over 75 million prevalent cases of cancers expected by 2030 (Ferlay et al., 2010). According to the 2011 United Nations high level committee on NCDs, the focus of many stakeholders has turned towards addressing the growing burden of cancer and other non-communicable diseases (NCDs) (Beaglehole et al., 2011), especially in Africa and other LMIC, where an existing high burden from infectious diseases has contributed to a double burden of disease (de-Graft Aikins et al., 2010b).

Over the last 20 years, an increasing trend has been observed in the incidence and deaths from different cancers globally, owing to changes in geographic and environmental features, lifestyles and behavioural changes, and the relatively poor response of the health system, especially in LMIC (Parkin et al., 2001b, Bray et al., 2012), see **Table 1.5** for details.

According to Parkin, there were 10.1 million new cancer cases and 6.2 million deaths in 2000, with Africa accounting for 6.3% and 6.4% of the global new cancer cases and deaths, respectively (Parkin, 2001). Parkin and colleagues reported that lung cancer was the main cancer globally with over 1.2 million new cases and 1.1 million

deaths, and breast cancer was the second most common with about 1.05 million new cases and about 373,000 deaths (Parkin et al., 2001b). Other top cancers were colorectal cancer with 876,000 new cases and 492,000 deaths, stomach cancer with 876,000 new cases and 647,000 deaths, and liver cancer with 564,000 new cases and 549,000 deaths, respectively (Parkin et al., 2001b). Oncologists have noted that the relatively favourable prognosis of breast cancer was due to better response from the health sector, and this has resulted in a relatively lower death rates compare to other cancers with higher incidence rates (Coleman et al., 2008).

In the 2002 GLOBOCAN study, reported estimates further underpinned the increasing burden of cancer globally (Parkin et al., 2005). Worldwide, there were 10.9 million new cancer cases and over 6.7 million deaths, and Africa accounted for about 6.0% and 7.5% of global new cancer cases and deaths, respectively (Parkin et al., 2005). From the report, lung cancer still presented with the highest burden with 1.35 million new cases and 1.18 million deaths, breast cancer had 1.15 million new cases and 411,000 deaths, colorectal cancer had 1.02 million new cases and 529,000 deaths, stomach cancer had 934,000 cases and 700,000 deaths, and liver cancer had 626,000 cases and 598,000 deaths. Again, breast cancer was the most prevalent cancer, with about 4.4 million survivors over a 5-year period.

Meanwhile, from the 2008 GLOBOCAN estimates, there were a total of 12.7 million new cancer cases and 7.6 million deaths, with Africa accounting for 5.6% and 7.1% of global new cancer cases and deaths respectively (Ferlay et al., 2010). For specific cancers, the pattern was still the-same with the estimates reported in 2000 and 2002. Lung cancer presented with the highest burden with 1.61 million new cases and 1.38 million deaths, breast cancer 1.38 million new cases and 458,000 deaths, colorectal cancer 1.23 million new cases and 608,000 deaths, stomach cancer had 989,000 cases and 738,000 deaths, and liver cancer had 748,000 cases and 696,000 deaths (Ferlay et al., 2010).

Table 1.5. Reported new cases and deaths for top five cancers globally (1990-2008)

Site	*1990 (estimates in millions) (Parkin et al., 1999)*		*2001 (estimates in millions) (Parkin et al., 2001b)*		*2002 (estimates in millions) (Parkin et al., 2005)*		*2008 (estimates in millions) (Ferlay et al., 2010)*	
	New cases	*Deaths*	*New cases*	*Deaths*	*New cases*	*Deaths*	*New cases*	*Deaths*
All	-	-	10.1	6.2	10.9	6.7	12.7	7.6
Lung	1.04	-	1.2	1.1	1.35	1.18	1.61	1.38
Breast	0.796	-	1.05	0.373	1.15	0.411	1.38	0.458
Colorectal	0.782	-	0.945	0.492	1.02	0.529	1.23	0.608
Stomach	0.798	-	0.876	0.647	0.934	0.7	0.989	0.738
Liver	0.437	-	0.564	0.549	0.626	0.598	0.748	0.696

Source: GLOBOCAN (Ferlay et al., 2010)

According to Soerjomatoram et al., about 169.3 million years were lost due to cancers in 2008, with colorectal, lung, breast and prostate cancers respectively being the main contributors to global DALYs (disability adjusted life years) (Soerjomataram et al., 2012). As noted above, the 2008 CONCORD study of cancers in 5 continents showed the 5 year survival rate was highest for breast cancer, followed by colorectal and prostate cancers, respectively (Coleman et al., 2008).

Cancer is increasingly becoming a major public health burden in Africa due to the rapid urbanization and associated lifestyle changes, increasing life expectancies, and high prevalence of HIV/AIDS (Jemal et al., 2012). It is believed that one out of five deaths from NCDs among people aged >45 years in Africa is caused by cancer (Parkin et al., 2008). The incidence of cancer in Africa varies across countries, and it is still difficult to say, with all certainty, the true incidence of cancer in many parts of Africa due to the lack of data (Bray et al., 2012). Experts still report that with the few data available, evidences are pointing to an increasing burden (Bray et al., 2012). In 2008, WHO reported that the annual diagnosis of cancer in Africa was estimated at

650,000 cases out of a total population of 965 million (Parkin et al., 2008). Variations have been observed in the patterns of cancers in Africa, especially between northern Africa and sub-Saharan Africa (SSA) (Morhason-Bello et al., 2013), as reports have shown that the burden of cancers is even rising at a faster rate in SSA compared to the northern parts of Africa due to relatively higher prevalence rates of infectious disease, unhealthy diets and poverty in SSA (World Health Organization, 2013a). WHO estimated about 551,000 new cases of cancer in sub-Saharan Africa (SSA) in 2008 with about 421,000 deaths (World Health Organization, 2013a). However, the GLOBOCAN 2008 study reported a total of 715,600 new cases of cancer and 541,800 deaths, with eastern Africa accounting for the highest burden at 221,000 new cancer cases and 173,700 deaths, followed by western Africa at 184,100 new cancer cases and 139,300 deaths (Ferlay et al., 2010), see **Table 1.6** for details.

Table 1.6. Distribution of new cancer cases and deaths in Africa

African region	***New cases (in 1000s)***			***Deaths (in 1000s)***		
	Men	***Women***	***Total***	***Men***	***Women***	***Total***
All Africa	324.9	390.7	715.6	267.0	274.8	541.8
Eastern Africa	100.8	120.2	221.0	85.4	88.3	173.7
Central Africa	29.5	37.4	66.9	25.6	27.6	53.2
Northern Africa	81.5	82.9	164.4	65.4	55.4	120.8
Southern Africa	40.6	38.6	79.2	29.3	25.5	54.8
Western Africa	72.5	111.6	184.1	61.3	78.0	139.3

Source: GLOBOCAN (Ferlay et al., 2010)

In the 1980s, cervical cancer was the main cancer among women, however with increasing life expectancy and better care for breast cancers, the prevalence of breast cancer is increasing in Africa due to presence of more survivors (Coleman et al., 2008). Experts have further reported that the incidence of cancer in Africa is changing with the spread of HIV in the region (Hirschhorn et al., 2012). The incidence rates of cervical cancer, Kaposi's sarcoma and non-Hodgkin's lymphoma (NHL), which are all AIDS-defining illnesses, have increased in the last two decades (Hirschhorn et al., 2012). According to Parkin et al., the top five cancers among women in Africa in 2008 were cervical cancer (23.3%), breast cancer (19.2%), Kaposi's sarcoma (5.1%), liver cancer (5.0%) and NHL (3.7%); while among men, liver cancer (14.8%), Kaposi's sarcoma (12.9%), prostate cancer (9.5%), bladder cancer (6.1%) and NHL (5.7%) were the top five cancers (Parkin et al., 2008). Morhason-Bello et al. reported that the incidence of breast cancer shows regional variation between northern Africa and SSA; breast cancer is the leading cancer among women in northern Africa, but second to cervical cancer in SSA (Morhason-Bello et al., 2013). In addition, prostate cancer was reported as the leading cancer among African men especially in the northern parts, while Kaposi's sarcoma was a leading cancer in SSA (Morhason-Bello et al., 2013, Center et al., 2012). As noted above, the variations between these two African regions further reflects the presence of infectious diseases in SSA, notably HIV/AIDS, and possibly reflects the higher prevalence rates of cervical cancer and Kaposi's sarcoma in SSA.

Challenges faced in Africa include late presentation of patients to health facilities (usually at advanced stages of the malignancy), poor and inappropriate treatment, high cost of medications, lack of adequate follow-up, and the innate social norms and beliefs (many people prefer herbal practitioners), poverty, and poor standards of living (Adebamowo and Akarolo-Anthony, 2009). Besides, another important problem is the lack of data and poor record keeping (Parkin, 2006a). Reports show that few countries have population-based cancer registries, with the few available data sourced from the few hospital-based registries, which are not regularly updated (Parkin, 2006a, Jedy-Agba et al., 2012). Largely, this has resulted in a poor response

from the health system, and obviously reflecting in greater morbidity and mortality rates in Africa compared to other world regions (Jemal et al., 2012). The global cancer study (GLOBOCAN) predicts that the global cancer burden will continue to increase and by 2030, developing world, especially Africa, will account for about 56% and 63% of new cancer cases and deaths, respectively (Ferlay et al., 2010).

Causes of cancer in Africa

The causes of cancers in Africa vary and have been linked to several factors, including ineffective health systems, poor living conditions, and poverty (Sitas et al., 2008). However, epidemiologists have reported that infections are the main causes of cancers in Africa, and was responsible for about 25.0-32.7% of new cancer cases in 2008 (Sitas et al., 2008, Ferlay et al., 2010).

Infections: HIV is a main cause of cancer in Africa, responsible for Kaposi's sarcoma, cervical cancer and other AIDS-defining cancers (Chokunonga et al., 1999). In 2007, 22.5 million people were living with HIV/AIDS in Africa, with the prevalence ranging from 5% in Nigeria to 38% in Botswana (Hirschhorn et al., 2012). HIV ranks among the leading causes of deaths in Africa, accounting for about 1.6 million deaths in 2007, with AIDS-defining cancers contributing hugely to this (Adebamowo and Akarolo-Anthony, 2009). Other infectious agents include Hepatis B & C viruses (liver cancers), Human Papiloma Virus (cervical cancer), Epstein Barr Virus (Burkitts lymphoma), helicobacter pylori (stomach cancer), Kaposi's Sarcoma-associated Herpes Virus, formerly HHV-8 (Kaposi's sarcoma and primary effusion lymphoma), Human T-lymphotropic Virus (adult T-cell leukemia), and human polyomaviruses (brain tumours and mesotheliomas) (Pagano et al., 2004).

Smoking and harmful use of alcohol: Tobacco is regarded the most preventable cause of cancer globally (Pampel, 2008). In Africa, the prevalence of smoking has been increasing, especially in the younger population age groups, owing to lack of effective government policies on tobacco sales and consumption (Pampel, 2008, Saloojee and Dagli, 2000). According to Pampel, the prevalence of smoking in Africa ranges between 8.0% in Nigeria to about 27.3% in Madagascar (Pampel,

2008). Moreover, the consumption of alcohol in many African countries is increasing (Pisa et al., 2010), with about 20-30% of liver cancers related to this (Sitas et al., 2008).

Unhealthy diets, physical inactivity and obesity: Due to the rapid urbanization in many African countries, there has been a corresponding increase in related western lifestyles, which are main risk factors for many NCDs, including cancers (Assah et al., 2011). In addition, many people are increasingly becoming physically inactive due to long sitting hours (mostly in offices), coupled with reduced walking and exercise (Assah et al., 2011). Consequently, there is increase prevalence of overweight and obesity. Besides, efforts towards enlightening people on the risks of obesity have been met with challenges, as this is seen as a sign of healthy living in some African settings (Cecchini et al., 2010). About 30-40% of cancers are related to unhealthy diets, physical inactivity and obesity (Sitas et al., 2008).

Industrialization and environmental pollution: In many African countries, there is virtually no policy on environmental pollution (Wichmann and Voyi, 2012). Carbon monoxide and many industrial toxic wastes are known carcinogens (Mortimer et al., 2012, Adebamowo and Akarolo-Anthony, 2009). Albrecht further reported that in some African settings, up to 90% of cancers may be due to chemicals released into the atmosphere from various sources of environmental pollution (Albrecht, 2011).

In view of the uncertainties surrounding the burden of cancers in Africa and the over reliance on GLOBOCAN estimates by researchers and stakeholders, it is important to conduct a detailed review of specific cancers in Africa towards attempting to provide improved estimate of the incidence in the region.

1.1.11 Chronic Respiratory Diseases

Globally, chronic respiratory diseases (CRDs) are among the top causes of deaths and disabilities among NCDs, accounting for 4.7% of global disability-adjusted life years (DALYs), of which chronic obstructive pulmonary disease (COPD) is responsible for about two-thirds (Murray et al., 2012). According to WHO global burden of disease (GBD) estimates, over 600 million people have allergic rhinitis, 300 million people have asthma, and 210 million people have COPD (World Health Organization, 2008). The WHO also estimates that COPD is responsible for about 3 million deaths globally in 2011, accounting for about 9.1% of all NCDs deaths (World Health Organization, 2011a). Globally, COPD is rated the fourth leading cause of death and by 2030, it is projected to become the third leading cause of death (World Health Organization, 2011a). Moreover, it is expected to overtake HIV/AIDS as the leading cause of death in Africa at this point (Bouayad et al., 2006). Worldwide, an estimated 300 million people are living with asthma, and current trends suggest that an additional 100 million people may be living with asthma by 2025; it has been rated the most common chronic disease affecting children (IUATLD, 2011). The World Health Organization (WHO) estimated about 250,000 deaths from asthma annually, mostly in low- and middle-income countries (LMIC) (Bousquet et al., 2010, Braman, 2006)

Chronic Obstructive Pulmonary Disease (COPD)

The increasing burden of COPD, and other respiratory diseases in Africa can be attributed to fast rates of urbanization, tobacco smoking, environmental pollution, exposure to combustion products of biomass fuels (from coal, firewood and agricultural residue), occupational dusts, tuberculosis, and long-term sequelae of childhood respiratory infections (van Gemert et al., 2011). Attempts at reducing this burden have been hindered mainly due to: inadequate standards of health promotion and other health services; insufficient attention from health planners, government regulators and media; absence of national guidelines on the management of COPD and lack of funds (Mehrotra et al., 2009, Finney et al., 2013). In fact, in many urban African settings, reports reveal an increasing consumption of tobacco products (van Gemert et al., 2011), which is made worse due to lack of government regulations on tobacco sales and use (Mehrotra et al., 2009). In some mixed, urban and rural settings, most households still use firewood and charcoal for domestic cooking and many countries are yet to implement control strategies for biomass fuel exposure (van Gemert et al., 2011, Finney et al., 2013). The treatment of COPD in many resource-poor settings has also been a huge challenge (Stanciole et al., 2012). Inhaled steroids, which are an effective treatment of COPD, have been included in the amended WHO list of essential medicines (van Gemert et al., 2011). However, these are mostly unavailable and/or unaffordable in many African settings (Nafti et al., 2009). In fact, policymakers in some African countries have stated that it may be unrealistic to assume that essential drugs for treating COPD and other CRDs can be given free to patients (Finney et al., 2013). This raises critical questions of equity and priority setting since drugs for HIV/AIDS and tuberculosis are typically supplied free in Africa (Mehrotra et al., 2009).

Moreover, there is a lack of standard treatment guidelines and protocols for the management of COPD, and when available, health workers have not been adequately trained to identify and treat the disease (IUATLD, 2011). Lung function assessment is vital to COPD diagnosis and in quantifying airflow obstruction, and this is often needed to differentiate COPD from other obstructive airway diseases (Mehrotra et

al., 2009). It has been reported that spirometer, peak flow meter, and simple lung function test apparatus are scarcely available in many African settings and most treatments have mainly been based on acute exacerbations rather than an overall disease management plan (Mehrotra et al., 2009, Abdool-Gaffar et al., 2011). Therefore, delayed diagnosis of COPD typically follows lengthy periods of hesitation from doctors and concerns raised by patients and their families (van Gemert et al., 2011).

The understanding of the epidemiology of COPD on the African continent is still very limited (Mehrotra et al., 2009). Although systematic reviews have been conducted on COPD in Africa (van Gemert et al., 2011, Mehrotra et al., 2009, Finney et al., 2013), only one of them is about the continent-wide burden of COPD while two other two focused on sub-Saharan Africa. These reviews mainly provided a systematic presentation of the available evidence, but there is still a need to further analyse the available studies to understand the appropriateness of the case definition used (spirometry vs non-spirometry data) and the effects of covariates such as sex, age, year of the study and country of the study. Researchers, policy makers and other stakeholders in Africa could be assisted with such information in designing further studies. Therefore, it is important to provide a deeper insight in the problem of COPD in Africa, by examining and comparing the two available types of data (spirometry-based and other) and investigating the role of covariates on the prevalence of COPD in Africa.

Asthma

Asthma is widely known as a multifactorial respiratory disorder with both genetic and environmental underlying risk factors (Bousquet et al., 2010). Exposure to common allergens (including pollens, dust mites and animal furs) and indoor and outdoor air pollution from various sources (e.g. traffic pollution, combustion of fossils and biomass fuels, workplace dust) have all been implicated as triggers of the disease (ECRHS, 2012). Second hand tobacco smoking is a confirmed risk factor in paediatric patients (Cazzoletti et al., 2010, van Gemert et al., 2011). Viral infections, a major cause of upper respiratory tract infections and "common cold", are also a common risk factor in children (Wong et al., 2010, Dagoye et al., 2003). As noted, helminthic infections are relatively common in Africa and are associated with bronchial hyper-responsiveness and asthma (Perzanowski et al., 2002, van Gemert et al., 2011); this is perhaps due to the presence of related raised immunoglobulin E (IgE) and a prominent Th2 immune response (van Gemert et al., 2011, Wjst and Boakye, 2007). The International Study of Asthma and Allergies (ISAAC) reported that asthma prevalence among children is increasing in Africa and has contributed most to the burden of disease through its effects on quality of life (Bousquet et al., 2010). In-patient admissions and purchase of medications account for most of the direct costs on government, while loss of productivity, due to absenteeism from work and school, are responsible for most of the indirect costs (Stanciole et al., 2012, Bahadori et al., 2009).

Studies on asthma are few in Africa, with most publications mainly from South African and Nigerian populations (Wjst and Boakye, 2007). One main factor affecting research output is the diagnosis of asthma, which still remains a challenging issue (Patel et al., 2008, Martins et al., 2009). The World Health Organization (WHO) has emphasized that this has limited on-going research efforts globally (Martins et al., 2009, Braman, 2006). The International Union against Tuberculosis and Lung Diseases (IUATLD) published one of the first diagnostic and survey guidelines for asthma in 1984, but experts subsequently reported concerns about its precision and reliability (Burney et al., 1989). According to the Global Initiative for

Asthma (GINA), detailed history, physical examination and spirometric lung function tests are vital to the diagnosis and management of asthma (Masoli et al., 2004, Cazzoletti et al., 2010). Generally, a reduction in forced expiratory volume in one second (FEV_1) and peak expiratory flow (PEF) may be indicative of asthma, with the amount of reduction proportional to the severity of asthma (Braman, 2006). GINA proposed that an increase in FEV_1 of >12% and 200ml in about 15-20 minutes following the inhalation of 200-400μg of salbutamol or a 20% increase in PEF from baseline can be employed as a standardized criteria in diagnosis of asthma (Cazzoletti et al., 2010). This, however, lacks sensitivity, as many asthmatics, especially those on treatment, may not exhibit an increase in FEV_1 and PEF when assessed (Martins et al., 2009, Ehrlich et al., 1998). Thus, although asthma is characterized by significant reversibility of airway obstruction, an absence of reversibility may not always exclude the presence of asthma (Ehrlich et al., 1998). The International Study of Asthma and Allergies in Childhood (ISAAC), established in 1991, remains the largest epidemiological study among children globally (IUATLD, 2011). ISAAC methodologies and scoring are currently the most widely employed by researchers in Africa (IUATLD, 2011, Braman, 2006). This involves both video and written questionnaires, as there were reports that video and pictorial representations of asthma symptoms may contribute to improved case recognition in younger children (IUATLD, 2011). However, this is still a subject of debate among experts (Wandalsen et al., 2009). The European Community Respiratory Health Survey (ECRHS), which assesses the prevalence of atopy and symptoms of airway disease among older age groups in Western Europe, has been widely implemented and has reported significant geographic variations in the prevalence of asthma and atopy (ECRHS, 2012). Despite these revised guidelines, both ISAAC and ECRHS research groups have reported challenges in achieving high sensitivity and specificity in case ascertainment with the symptom "wheeze at rest in the last12 months" (also regarded as current wheeze, or active wheeze) yielding the highest sensitivity and specificity (IUATLD, 2011).

In Africa, problems including those arising from the over-utilization of health services, lack of trained staff and diagnostic apparatus, and non-availability and

unaffordability of inhaled medications have hindered efforts to improve the management of asthma (Musafiri et al., 2011b, Uijen et al., 2008). The lack of organized health promotion programmes, such as effective control strategies for environmental triggers, air pollutants, and occupational dusts have also contributed to the growing burden (Reddel et al., 2009). The WHO has reported that the levels of asthma control and health responses in the continent have been below recommended standards, and that these have contributed to the size of the disease burden (Bousquet et al., 2010, Braman, 2006). In addition, although many African countries have national guidelines for the management of asthma and other CRDs, these guidelines have not been implemented in most rural areas (Mash et al., 2009, Ait-Khaled et al., 2007a). Economic analyses in many African settings have shown that direct costs from asthma are usually greater than the indirect costs. However, indirect costs represent a relatively higher proportion of total costs among paediatric than in adult patients (Stanciole et al., 2012). Moreover, the wider economic burden on individuals, families, employers and society, due to loss of future potential source of livelihood, has also been devastating in many resource-poor settings (Musafiri et al., 2011b). It is believed that many children with asthma in Africa may fail to achieve their full potential if proper management and control measures are not put in place (IUATLD, 2011). It has been suggested that education of healthcare providers and the public is a vital element of the response to the challenge posed by asthma in Africa (Braman, 2006, Ndiaye et al., 2004).

An increase in world's urban population from 45% to 59% is expected by 2015, with over half of this occurring in Africa (Stanciole et al., 2012). It is also expected that the prevalence of asthma and many chronic diseases in Africa will increase due to this growing population size and from effects of accompanying urbanization and adoption of western lifestyles (Beaglehole, 2011). In light of this, and of the low research output and poor availability of health services data on the burden of asthma in Africa, it is important to analyse the available data through a systematic review of the literature in order to attempt to quantify the burden, guide health priority settings and inform the formulation of an appropriate health policy response.

1.2 AIM AND OBJECTIVES

As identified under the *gaps in information, control and response to NCDs in Africa*; the understanding of the burden of NCDs in Africa is presently quite poor due to the relative lack of data and low level of research on NCDs in the continent. Africa has recently seen large increase in life expectancy and urbanization, all of which is driving the NCD burden in the continent. Experts believe underestimation of disease burden in many parts of Africa may be inevitable due to extrapolation and over-modelling of the scarce data (King and Bertino, 2008). It is also evident that some studies reporting the burden of NCDs in Africa are derived from modelling based on data from other countries imputed into African countries, and may not be strictly based on data originating from Africa itself (Kirigia and Barry, 2008). This is in stark contrast with the need to have useful information on NCDs, with particular focus on data derived from Africa, according the UN's political prioritization of NCD burden (Beaglehole et al., 2011). This thesis will, therefore, be focussing on understanding the prevalence, and/or where there are available data, the incidence, of four major NCDs in Africa, which have contributed highly to the burden of NCDs, not only in Africa, but also across the world.

I have chosen to estimate the prevalence of NCDs mainly because data on these are far more available across Africa than data on other measures of disease burden (including deaths, DALYs and risk factors). Second, the IHME has been involved in estimation of mortalities and morbidities (mainly DALYs) of diseases globally, but their estimates of disease prevalence have not been made public. Additionally, their sources of data, from which disease prevalence rates could have been estimated, are hardly available. Third, due to availability of more data on NCD prevalence in Africa, the health service consequence and the overall response from governments of many African nations have been driven more by the few available data on NCD prevalence. It is therefore important to systematically review all available evidence and gather more data aimed at arriving at an improved estimate of the prevalence of NCDs in Africa that fairly represents the African population, towards prompting better and appropriate policy response across the continent.

1.2.1 Aim

This thesis aims to systematically review available literature on NCDs in Africa, gather and critically appraise available evidence, and provide a population representative estimate of the prevalence and/or incidence of major non-communicable diseases in Africa. This thesis will mainly review and provide estimates for the four major non-communicable diseases in Africa, which have earlier been identified as the leading NCDs in the continent according to the WHO GBD estimates. These are: cardiovascular diseases (hypertension and stroke), diabetes, major cancers, and chronic respiratory diseases (COPD and asthma).

1.2.2 Objectives

The objectives are:

i. To conduct a systematic search and provide detailed review of literature (published and unpublished) on four major NCDS in Africa;

ii. To provide estimates of the prevalence and/or incidence of four major NCDs in Africa using an epidemiological model and the United Nation population demographics, and critically discuss the findings; and

iii. To discuss *i* and *ii* in terms of the gaps in information, control and response to NCDs in Africa, and suggest ways to address these in the continent.

2 METHODS

2.1 OVERVIEW

This chapter describes the methodologies applied in this dissertation, which have been categorized according to each broad NCD under review, namely: Cardiovascular Diseases (hypertension and stroke), Diabetes, Cancers, and Chronic Respiratory Disease (COPD and Asthma). Generally, the method employed for each systematic review follows the pattern below:

i. Search strategy and data sources: This is a summary of how searches were conducted and the databases sourced. Tables of search terms are included in this section.

ii. Study selection criteria: This describes the process of study selection, including the inclusion and exclusion criteria, respectively.

iii. Quality criteria and grading: This explains how selected studies were graded in terms of the quality of individual studies.

iv. Case definitions: This gives an overview of various case definitions on the selected NCD.

v. Data extraction: This is a description of the collation and extraction of data from selected studies

vi. Data analysis: This describes how the extracted data were analysed and the modelling applied for the estimation of disease prevalence and cases.

2.2 CARDIOVASCULAR DISEASES

2.2.1 Hypertension

Search strategy and data sources

After identifying Medical Subject Headings (MESH) and keywords following consultations with a librarian, a final search strategy was developed. A systematic search of Medline, EMBASE and Global Health was conducted, with publication dates set from January 1980 up to December 2013. The list of African countries included in the searches was based on the World Bank list of economies (October 2013) (World Bank, 2014b). A further search was conducted on Google Scholar to identify unpublished studies. Experts on cardiovascular research in Africa were also contacted to seek their opinion on relevant African databases, links and websites. For identified key authors and relevant search terms, an e-mail alert was registered and new publications were automatically sent to my e-mail. Hand-searching of reference lists of relevant publications, and key journals, were finally done to identify more studies that could have been omitted from the databases' searches. The search terms employed on Medline are shown in **Table 2.1,** while search terms for EMBASE and Global Health are shown in **Appendix 1a** and **1b**, respectively.

Table 2.1. Search terms for studies on hypertension in Africa (Medline)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp hypertension/ or peripheral vascular diseases/ or elevated blood pressure/ or cardiovascular diseases/ or heart diseases/ or borderline hypertension
13	Hypertensive heart disease.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
14	12 or 13
15	1 and 11 and 14
16	limit 15 to (humans and yr="1980 -Current")

Study selection criteria

The inclusion criteria were:

i. Original population-based, cohort or cross-sectional studies on hypertension;

ii. Studies conducted in urban, rural, or mixed settings mainly within African population groups;

iii. Studies providing numerical estimates on the prevalence and / or awareness of hypertension; and

iv. Studies that provided clearly defined, unambiguous methodologies.

The exclusion criteria were:

i. Studies that were mainly hospital-based;

ii. Studies that had non-human subjects;

iii. Studies conducted before 1980; and

iv. Studies that were mainly reviews, viewpoints or editorials.

No language restrictions were applied.

Quality criteria and grading

Quality of studies was assessed based on the following criteria:

i. *Study design*: Under this, flaws in the design and execution of study were examined. Basically, this assesses methods of estimation of sample size and sampling methods across studies, and the methods of dealing with design specific issues such as: training of study investigators, adherence to standardized protocol for blood pressure measurement (**Box 2.1**), pre-testing and reviewing questionnaires before data entry, and addressing recall and interviewer's bias appropriately;

ii. *Study analysis*: This assesses the appropriateness of statistical and analytical methods employed across studies in the estimation of hypertension prevalence;

iii. *Study limitations*: This assesses if the study stated the limitations, as this may further guide in the choice of selection; and

iv. *Generalizability to the African population*: This broadly assesses if the sample size was representative of a larger population that can be generalized to the total African population

For the quality grading, I adapted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines (Balshem et al., 2011), as follows:

i. *High quality*: Studies with the entire four criteria, or any three including "study design", highlighted above well represented;

ii. *Moderate quality*: Studies with any three of the four criteria, or any two including "study design", highlighted above well represented;

iii. *Low quality*: Studies with any two of the four criteria, or "study design" only, highlighted above well represented; and

iv. *Very low quality*: Studies with only one (excluding "study design") or none of the four criteria highlighted above well represented.

As a basic rule, all studies that were graded as *high and moderate quality* were included in the quantitative analysis. Some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, and were described further in the discussion section. However, all *very low quality* studies have been excluded from the review.

Case definitions

The Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC) and the World Health Organization/ International Society of Hypertension (WHO/ISH) have provided clearer definitions of hypertension with appropriate staging of severity (JNC, 1997, JNC, 2003, Whitworth, 2003). Hypertension in adults is generally defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, with measurements taking on two or more blood pressure readings taken at each of two or more visits after initial screening.

Based on the general definition above, diagnostic criteria in the selected studies needed to comply with the following:

i. the sixth and seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 6 & 7) (JNC, 1997, JNC, 2003); and/or

ii. the 1999 and 2003 World Health Organization/ International Society of Hypertension (WHO/ISH) definitions and classification of blood pressure levels (Whitworth, 2003).

See **Table 2.2** for details of classification of blood pressures in adults, and **Box 2.1** for summary of blood pressure measurement protocols.

Table 2.2. Classification of blood pressure for adults

Category	*JNC*				*WHO/ISH*			
	6		**7**		**1999**		**2003**	
	SBP	**DBP**	**SBP**	**DBP**	**SBP**	**DBP**	**SBP**	**DBP**
Optimal	<120	and <80	-	-	<120	<80	-	-
Normal	120-129	and 80-84	<120	and <80	<130	<85	-	-
Borderline (JNC) / or High Normal (WHO/ISH)	130-139	or 85-89	120-139 (Pre-hypertension)	or 80-89 (Pre-hypertension)	130-139	85-89	-	-
Hypertension (JNC) / Grade 1 (WHO/ISH)	≥140	or ≥90	≥140	or ≥90	140-159	90-99	140-159	90-99
Stage 1 (JNC) / or Subgroup Borderline (WHO/ISH)	140-159	or 90-99	140-159	or 90-99	140-149	90-94	-	-
Stage 2 (JNC) / or Grade 2 (WHO/ISH)	160-179	or 100-109	≥160 (Stage 2)	or ≥100 (Stage 2)	160-179	100-109	160-179	100-109
Stage 3 (JNC) / or Grade 3 (WHO/ISH)	≥180	or ≥110	-	-	≥180	≥110	≥180	≥110

JNC: Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure, WHO/ISH: World Health Organization/ International Society of Hypertension, SBP: systolic blood pressure, DBP: diastolic blood pressure

Box 2.1. The JNC standard blood pressure measurement protocol (Source: (JNC, 1997, JNC, 2003))

1. Subjects should be seated in a chair with their backs supported and their arms bared and supported at heart level. Subjects should refrain from smoking or ingesting caffeine during the 30 minutes preceding the Measurement
2. Blood pressure measurement should begin after at least 5 minutes of rest
3. The appropriate cuff size must be used to ensure accurate measurement. The bladder within the cuff should encircle at least 80 percent of the arm. Many adults will require a large adult cuff
4. Measurements should be taken preferably with a mercury sphygmomanometer; otherwise, a recently calibrated aneroid manometer or a validated electronic device can be used
5. Both SBP and DBP should be recorded. The first appearance of sound (phase 1) is used to define SBP. The disappearance of sound (phase 5) is used to define DBP
6. Two or more readings separated by 2 minutes should be averaged. If the first two readings differ by more than 5 mm Hg, additional readings should be obtained and averaged.

Defining the awareness of hypertension

As noted in the introduction, many studies on hypertension in Africa have reported that patients were mostly unaware of their hypertension status, with hypertension diagnosed when they present in hospital for unrelated ailments. I therefore think it may be worthwhile in this review to include estimates on the general awareness of hypertension in Africa. An understanding of the awareness rate of hypertension may, in fact, be relatively reflective of the control and treatment response to hypertension across many African settings. Therefore, for the purpose of estimating the awareness rate of hypertension in this review, awareness of hypertension was defined as self-report by respondents of any prior diagnosis of hypertension by a doctor or certified health care professional, and excluding women diagnosed during pregnancy, as described by the WHO (Whitworth, 2003).

Data extraction

All extracted data were stored in 2010 Microsoft Excel file format. To allow for consistency, a parallel search (and double extraction) was conducted. Data were abstracted systematically on sample size, mean age or age range, number of hypertension cases, and the respective age- and sex-specific prevalence rates. These were sorted into mixed, urban and rural settings (based on studies that reported them). For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were included in the selected paper.

Data analysis

A random effects meta-analysis (DerSimonian and Laird method) was conducted on extracted crude prevalence and awareness rates of hypertension (DerSimonian and Laird, 1986). This was reported separately for mixed, urban and rural settings, all expressed as percentages. As there were more data points to allow for detailed analysis, these were then further categorized into 1990, 2000 and 2010, as obtained from studies conducted before 1995, from 1995 to 2004, from 2005 to 2013, respectively.

Rationale for choosing random effects meta-analysis

As discussed in the '*Introduction*' under '***Section 1.1.3**- Heterogeneities within and between African population subgroups*', Africa consists of diverse groups of people each with specific demographic characteristics, including those related to residence (urban versus rural), age distribution, ethnicity and culture, GDP and income status. I also stated that these need to be carefully considered in the estimation of disease burden in Africa, and indeed, any population group. One other factor is the lack of data and low research output on NCDs in Africa, meaning that a good number of the included studies were selected following rigorous systematic literature search. Even with a thorough quality grading of included studies, some of the selected studies may not be of high quality. Furthermore, characteristics of study populations differ widely across studies. Other sources of variations include study designs, sampling, case definitions, and statistical analysis, among others. Therefore, an ideal analysis that involves pooling estimates from various studies must account for these heterogeneities, and each measure of heterogeneity can then further assist in appropriately interpreting the estimates reported. One meta-analytic approach that fits these conditions is the Random Effects Model described by DerSimonian and Laird (DerSimonian and Laird, 1986). In the random effects model, the assumption is that the true effect size varies across studies and that the studies included represent a random sample of the effect sizes (prevalence estimates) that could have been observed. In this model, a small study is not discounted by giving it a small weight and a large study is not over-represented by giving it a large weight (which is what is observed in a fixed effect model). In other words, the pooled (summary) prevalence is estimated from a range of studies while avoiding that this pooled estimate is influenced by specific characteristics in an individual study. This is further noted in the *study limitations*.

The use of weighted means

In the estimation of overall systolic and diastolic blood pressure (SBP and DBP), *weighted means* were applied. The *'weighted*' in this context does not refer to the whole of the African population or the country population in which the study was

conducted. It mainly implies the use of respective sample sizes reported in each study to arrive at the SBP and DBP, i.e. the estimated mean SBP and DBP is weighted towards the sample size. Thus, the estimated SBP and DBP is only representative of the study samples. The import of this is that when large samples dominate selected studies (or data points), and those large samples do not represent the larger country or regional population, extrapolating these data to the whole of Africa may therefore need to be interpreted with caution. This is also noted in the *discussion*.

Analysing the awareness rate of hypertension

As noted above, awareness of hypertension was defined as number of people who reported being aware of their hypertension status. From each study, awareness rate of hypertension was estimated as number of people who reported being hypertensive, expressed as a percentage of total number of people in the study population adjudged to have hypertension. Pooled awareness rates of hypertension for 1990, 2000, and 2010, and rates across mixed, urban and rural settings were estimated, respectively.

Description of the modelling

For the modelling and estimation of hypertension cases in Africa, a meta-regression epidemiological model was developed, and applied on crude prevalence rates, sample sizes and respective mean age from all data points. See **Appendix 2** for all data used in modelling.

General approach to the meta-regression epidemiological modelling: In this model, all data points (mainly the crude prevalence rates and mean age) were plotted on a graph on Microsoft Excel, with all extracted crude prevalence rates plotted on the *y*-axis, i.e. dependent variable, and mean ages corresponding to each prevalence rate are plotted on the *x*-axis, i.e. independent variable. To account for variation in sample sizes from each data point, bubbles were generated on the graph, with the size of each bubble corresponding to the respective sample size reported (see **Figure 2.1**).

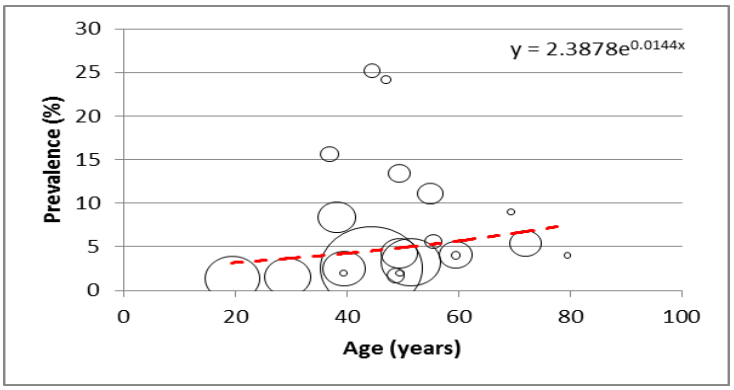

Figure 2.1. A template of the meta-regression epidemiological model

Although, it is well known that the prevalence of many NCDs in the population significantly increases with age (Anderson, 1999), the relationship between age and the disease may not be necessarily linear. Therefore I experimented with the models based on linear, logarithmic, exponential, Poisson, polynomial, power function and moving average statistical analyses, respectively, and chose the one which was the most predictive, i.e. in which the proportion of variance (R^2) of the disease prevalence explained by age was the greatest. In most cases, this was power function or exponential, but there were also diseases where linear or polynomial relationship showed better prediction and were used instead.

The use of mean age or age-specific prevalence estimates in the modelling

As noted, the model was based explicitly on age. A preferred approach would have been to use all the age-specific estimates from a study. However, not all studies reported age-specific prevalence estimates. Many studies reported single age estimates (usually the mean age of the study population) without mentioning what the prevalence looks like across various age groups in the population. Thus, in the model, I applied the mean age (or the single age) when only this was reported, and if a study reported age-specific estimates across the population, all these age-specific estimates were incorporated into the model. The disadvantage of using mean age only is that some selected studies do have extreme ages in the study population (very old and very young). This, therefore, automatically renders the mean age inappropriate. The use of mean age can only be truly appropriate when the study

population is normally distributed. In an actual research context, however, this is not the case. This is noted further in the *study limitations*.

Best fit for hypertension prevalence estimation: On the epidemiological model for hypertension, a trend-line was inserted, and the fitted curve explaining the largest proportion of variance (best fit) was applied. In this particular model the best fit applied was exponential, and this was used in the estimation of hypertension prevalence and cases in Africa. The equation generated from the fitted curve was then used to determine the prevalence of hypertension in Africa at midpoints of the United Nations (UN) population 5-year age-group population estimates for Africa, for the years 1990, 2000, 2010, respectively (United Nations, 2013).

Equation: This implies that prevalence of hypertension and corresponding cases (for the ages 20 years and above, which were predominantly the age groups from most studies) were estimated based on the UN population estimates for Africa for the ages 20-24, 25-29, 30-34, etc, at midpoints 22, 27, 32, etc. Therefore, if the equation generated from the actual epidemiological analysis was the same as that in the template model above (i.e. $y = 2.3878e^{0.0144x}$), then y = estimated prevalence (%); x = midpoints of UN age group. Hence, **Equation 1** gives the estimated number of hypertension cases. All statistical analyses were conducted on 2010 Microsoft Excel and Stata 13.1 (Copyright 1985-2013 Stata Corp LP).

Equation 1

Number of hypertension cases in Africa in 2010 =

y × UN population for Africa in 2010 / 100

For the calculation of Confidence Interval (CI) of the prevalence rates, I applied the Kirkwood and Sterne Confidence Interval for Rate (Kirkwood and Sterne, 2003), page 238, see **Equation 2.**

Equation 2

95% CI (prevalence) = (prevalence/EF) to (prevalence×EF)

Where EF= Error Factor= exp(1.96/√hypertension cases)

2.2.2 Stroke

Search strategy and data sources

Following initial consultation with a librarian, and identification of relevant Medical Subject Headings (MESH) and keywords, a final search strategy was developed. A systematic search of Medline, EMBASE and Global Health was conducted, with publication dates set from 1970 up to December 2013 (to allow for screening of more studies). A further search was conducted on Google Scholar. The list of African countries included in the searches was based on the World Bank list of economies (October 2013) (World Bank, 2014b). Experts on cardiovascular research in Africa were also contacted to seek their opinion on key journals and relevant African databases, links and websites. For identified key authors and relevant search terms, an e-mail alert was registered and new publications were automatically sent to my e-mail. Hand-searching of reference lists of relevant publications, and key journals, were finally done to identify more studies that could have been omitted from the databases' searches. The search terms employed on Medline are shown in **Table 2.3,** while search terms for EMBASE and Global Health are shown in **Appendix 1c** and **1d**, respectively.

Table 2.3. Search terms for studies on stroke in Africa (Medline)

#	***Search terms***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	stroke/ or brain infarction/ or brain stem infarctions/ or cerebral infarction/ or stroke, lacunar/
13	cerebrovascular accident/ or intracranial haemorrhage/ or hemorrhagic stroke/ or subarachnoid haemorrhage
14	cerebrovascular disease.mp.
15	CVA.mp.
16	12 or 13 or 14 or 15
17	1 and 11 and 16

Selection criteria

The inclusion criteria were:

i. Original population-based (cohort, cross-sectional or community door-to-door surveys), demographic health surveys, hospital records and outpatient clinics studies on stroke (this wide variety was allowed for due to paucity of data);

ii. Studies conducted in urban, rural, occupational, or mixed settings mainly within African population groups;

iii. Studies providing numerical estimates on the incidence and/or prevalence of stroke; and

iv. Studies that provided clearly defined, unambiguous methodologies.

The exclusion criteria were:

i. Studies that had non-human subjects;

ii. Studies conducted before 1970 (also allowed for due to paucity of data); and

iii. Studies that were mainly reviews, viewpoints or editorials.

No language restrictions were applied.

Quality criteria and grading

Quality of studies was assessed based on the following criteria:

i. *Study design*: Under this, flaws in the design and execution of study were examined. Basically, this assesses methods of estimation of sample size and sampling methods across studies, and the methods of dealing with design specific issues such as: training of study investigators, adherence to standardized protocol for identifying stroke cases in the population, pre-testing and reviewing questionnaires before data entry, and addressing recall and interviewer's bias appropriately;

ii. *Study analysis*: This assesses the appropriateness of statistical and analytical methods employed across studies in the estimation of the incidence and/or prevalence of stroke;

iii. *Study limitations*: This assesses if the study stated the limitations, as this may further guide in the choice of selection; and

iv. *Generalizability to the African population*: This broadly assesses if the study site was representative of a larger population that can be generalized to the total African population

For the quality grading, I adapted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines (Balshem et al., 2011), as follows:

i. *High quality*: Studies with the entire four criteria, or any three including "study design", highlighted above well represented;

ii. *Moderate quality*: Studies with any three of the four criteria, or any two including "study design", highlighted above well represented;

iii. *Low quality*: Studies with any two of the four criteria, or "study design" only, highlighted above well represented; and

iv. *Very low quality*: Studies with only one (excluding "study design") or none of the four criteria highlighted above well represented.

As a basic rule, all studies that were graded as *high and moderate quality* were included in the quantitative analysis. Some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, and were described

further in the discussion section. However, all *very low quality* studies have been excluded from the review.

Case definitions

As noted in the introduction, diagnosis of stroke on population wide scale has proved difficult to researchers (this is highlighted further in the discussion). Across many studies, subjects were asked on symptoms suggestive of previous episodes of stroke or cerebrovascular events, and if diagnosed by a doctor. This included sudden weakness of any part of the body, difficulty in speaking, raising hands or walking, blurred vision, etc., and this were linked to the WHO definition of stroke to make a diagnosis.

Based on this understanding, the final stroke case ascertainment complied with the following:

i. WHO definition, defined as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting longer than 24 hour, unless interrupted by death, with no apparent cause other than that of vascular origin" (Hatano, 1976, WHO MONICA Project Investigators, 1988); and/or

ii. Studies in which recovery within 24 hours were highlighted, such as those that excluded Transient Ischemic Attack, defined as "an acute loss of focal cerebral or ocular function with symptoms lasting less than 24 hours and which after adequate investigation is presumed to be embolic or thrombotic vascular disease" (Hatano, 1976, WHO MONICA Project Investigators, 1988).

New cases of stroke were defined as number of people presenting with first ever stroke in a given period, while stroke survivors were the total number of people who have had stroke or living with its sequelae at a given time (World Health Organization, 1990, WHO MONICA Project Investigators, 1988).

Data extraction

All extracted data was stored in a 2010 Microsoft Excel file format. Data were abstracted systematically on study location, study period, mean age or age range, person years or sample size, incident cases of stroke or number of stroke survivors, and their respective age- and sex-specific incidence or prevalence rates. These were sorted into population-based or hospital-based data separately for analysis. For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were compared for consistency and included in the selected paper.

Data analysis

From reported overall crude incidence or prevalence of stroke in a given cohort, a random effect meta-analysis was conducted with pooled effect of stroke expressed per 100,000 person years or population respectively (DerSimonian and Laird, 1986). The rationale for using random effects meta-analysis has been earlier described. Each measure of heterogeneity and appropriateness of combining heterogeneous studies is further described under *study limitations*. The overall estimates of age- and sex-specific prevalence and incidence from all studies were used in the epidemiological modelling (**Appendix 3**). The use of age-specific estimates and mean age (and limitations) has been highlighted earlier. This is further described under *study limitations*.

Description of the modelling

The general approach to the epidemiological modelling has already been described. In this particular model, exponential function was used for the estimation of stroke incidence and prevalence rates as it showed the greatest prediction power. The equations generated from the modelled curves were then separately used to estimate the new cases of stroke and number of stroke survivors in 2010 at midpoints of the United Nation (UN) population 5-year age groups (United Nations, 2013), see **Equation 3**. Africa populations were determined from the 2012 United Nations population demographics (United Nations, 2013). This further implies that

prevalence of stroke and corresponding cases (for the ages 20 years and above, which were predominantly the age groups from most studies) were estimated based on the UN population estimates for Africa for the ages 15-19, 20-24, 25-29, 30-34, etc, at points 17, 22, 27, 32, etc. See **Appendix 3** for all data used in modelling. All statistical analyses were conducted on 2010 Microsoft Excel and Stata 13. 1 (Copyright 1985-2013 Stata Corp LP)

Equation 3

Number of new stroke cases (stroke survivors) in Africa in 2010 =

Estimated incidence (or prevalence) from epidemiological model × UN population for Africa in 2010 / 100000

For the calculation of Confidence Interval (CI), I applied the Kirkwood and Sterne Confidence Interval for Rate (Kirkwood and Sterne, 2003), page 238, see **Equation 2.**

2.3 DIABETES

Search strategy and data sources

An initial consultation with a librarian was done, and following identification of Medical Subject Headings (MESH) and keywords, a final search strategy was drafted. A systematic search of Medline, EMBASE and Global Health was conducted, with publication dates set from 1980 up to December 2013. A further search was conducted on Google Scholar. The list of African countries included in the searches was based on the World Bank list of economies (October 2013) (World Bank, 2014b). Experts on endocrinology and diabetes research in Africa were also contacted to seek their opinion on key journals and relevant African databases, links and websites. For identified key authors and relevant search terms, an e-mail alert was registered and new publications were automatically sent to my e-mail. Hand-searching of reference lists of relevant publications, and key journals, were finally done to identify more studies that could have been omitted from the databases' searches. The search terms employed on Medline are shown in **Table 2.4,** while search terms for EMBASE and Global Health are shown in **Appendix 1e** and **1f**, respectively.

Table 2.4. Search terms for studies of diabetes in Africa (Medline)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp glucose metabolism disorders/ or exp diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ or exp diabetes, gestational/ or exp diabetic ketoacidosis/ or exp prediabetic state/ or exp glycosuria/ or exp hyperglycemia/ or exp glucose intolerance/
13	1 and 11 and 12

Study selection criteria

The inclusion criteria were:

i. Original population-based, cohort or cross-sectional studies on diabetes, Impaired Glucose Tolerance (IGT) or Impaired Fasting Glycemia (IFG) ;

ii. Studies conducted in urban, rural or mixed settings mainly within African population groups;

iii. Studies providing numerical estimates on the prevalence of diabetes, IGT or IFG; and

iv. Studies that provided clearly defined, unambiguous methodologies.

The exclusion criteria were:

i. Studies that were hospital-based;

ii. Studies that had non-human subjects;

iii. Studies conducted before 1980; and

iv. Studies that were mainly reviews, viewpoints or editorials.

No language restrictions were applied.

Quality criteria and grading

Quality of studies was assessed based on the following criteria:

i. *Study design*: Under this, flaws in the design and execution of study were examined. Basically, this assesses methods of estimation of sample size and sampling methods across studies, and the methods of dealing with design specific issues such as: training of study investigators, adherence to standardized protocol for blood glucose measurement in epidemiological surveys, pre-testing and reviewing questionnaires before data entry, and addressing recall and interviewer's bias appropriately;

ii. *Study analysis*: This assesses the appropriateness of statistical and analytical methods employed across studies in the estimation of the prevalence of diabetes, IGT or IFG;

iii. *Study limitations*: This assesses if the study stated the limitations, as this may further guide in the choice of selection; and

iv. *Generalizability to the African population*: This broadly assesses if the study site was representative of a larger population that can be generalized to the total African population

For the quality grading, I adapted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines (Balshem et al., 2011), as follows:

i. *High quality*: Studies with the entire four criteria, or any three including "study design", highlighted above well represented;

ii. *Moderate quality*: Studies with any three of the four criteria, or any two including "study design", highlighted above well represented;

iii. *Low quality*: Studies with any two of the four criteria, or "study design" only, highlighted above well represented; and

iv. *Very low quality*: Studies with only one (excluding "study design") or none of the four criteria highlighted above well represented.

As a basic rule, all studies that were graded as *high and moderate quality* were included in the quantitative analysis. Some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, and were described further in the discussion section. However, all *very low quality* studies have been excluded from the review.

Case definitions

Generally, many have stated that diagnosis of diabetes appear quite straight forward as this could be based on blood glucose values following overnight fast or 2 hours after a 75g oral glucose challenge (OGTT) (Mbanya and Ramiaya, 2006). However, in the conduct of epidemiological surveys, several other factors including blood sample collection and medical history, among others, need be considered to ensure standard diagnostic protocols are followed (Sobngwi et al., 2001).

According to IDF, diabetes is a chronic metabolic condition, usually characterized by raised blood glucose, resulting from impairment in secretion of insulin, its action, or both (International Diabetes Federation, 2000, International Diabetes Federation, 2003, International Diabetes Federation, 2006, International Diabetes Federation,

2009). Diabetes presents in various forms in humans, the three main categories are type 1, type 2 and gestational diabetes, respectively (Sobngwi et al., 2001). Type 1 diabetes has autoimmune aetiology, usually from destruction of pancreatic beta cells, with consequent loss of production of insulin; previously referred to as insulin dependent diabetes mellitus (IDDM) (Mbanya et al., 2006). Type 2 diabetes results from insulin resistance, and or, abnormal insulin secretion; this was also previously referred to as non-insulin dependent diabetes mellitus (NIDDM) (Mbanya and Ramiaya, 2006). Gestational diabetes mellitus is generally described as any degree of blood glucose intolerance diagnosed first during pregnancy (Jiwani et al., 2012). Type 2 diabetes is also characterized by intermediate hyperglycaemic episodes, namely Impaired Glucose Tolerance (IGT) and Impaired Fasting Glycemia (IFG). IGT is an elevated non-diabetic levels of blood glucose, and can be confirmed 2 hours following a 75g oral glucose tolerance test (OGTT), while IFG is an elevated non-diabetic fasting blood glucose (World Health Organization, 2006). IGT and IFG have both been reported as transitional stages in the development of type 2 diabetes (Mbanya and Ramiaya, 2006).

Most survey and diagnostic criteria for diabetes have been based on WHO 1980, 1985 and 1998 criteria respectively (Mbanya et al., 2010, World Health Organization, 1985, Alberti and Zimmet, 1998). In 1997, the American Diabetic Association (ADA) proposed diagnostic criteria for clinical and epidemiological studies; this was revised in 2003 (Gabir et al., 2000, Levitt et al., 2000). Experts have examined their predictive values during epidemiologic surveys (Kumar, 2002, Levitt et al., 2000); for example, Gabir and colleagues reported from a study of 5,023 Indian adults using fasting plasma glucose (FPG) and 2-hour post load plasma glucose (2-h PG) concentrations, that the prevalence of diabetes using 1997 ADA criteria was 12.5%, much lower than 1985 WHO criteria (14.6%) and 1998 WHO criteria (15.3%) (Gabir et al., 2000). They further discovered that both FPG and 2-h PG have almost the same predictive values, and the observed prevalence of IFG and IGT could help at early identification of people at high risk of diabetes. In 2006, WHO and IDF spelled out recommendations for diabetes epidemiological surveys and clinical diagnosis- Diabetes was defined as FPG $\geq$7.0mmol/l (126mg/dl) or a 2-h

PG ≥11.1mmol/l (200mg/dl); IGT defined as FPG <7.0mmol/l (126mg/dl) or a 2-h PG 7.8-11.1mmol/l (140-200mg/dl); and IFG was given as FPG 6.1-6.9mmol/l (110-125mg/dl) or a 2-h PG <7.8mmol/l (140mg/dl) (World Health Organization, 2006). The committee further recommends that venous plasma glucose should be gold standard for measuring and reporting blood glucose values, while conversion estimates may be employed for capillary glucose, which is commonly used in low resource settings. In addition,bar 2-h PG following an oral glucose tolerance test (OGTT) should still be employed in diagnosing diabetes, as FPG may give a false negative results in about 30% of cases, while emphasizing that OGTT remains the only means of diagnosing people with IGT (World Health Organization, 2006).

The use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes is thought to be a better predictor of micro- and macro-vascular events compared to FPG or 2-hPG following a 75g OGTT (Mbanya and Ramiaya, 2006). Other advantages include its ability to reflect the mean plasma glucose in an individual over a period of 2 to 3 months, its ease of conduct, and ability to carry out the test at any time of the day (Sobngwi et al., 2001). However, there are still no sufficient evidence on the use of glycated haemoglobin (HbA1c) in population studies based in Africa, as HbA1c is thought to be very expensive to carry out on a population-wide scale (Mbanya et al., 2010, World Health Organization, 2011d). Refer to **Table 2.5** for details of diabetes diagnostic criteria.

Therefore based on the above, the final case definition for retained studies needed to comply with:

i. WHO 1985 or 1998 diabetes diagnostic criteria; or

ii. ADA 1997 or 2003 diabetes diagnostic criteria; and/or

iii. WHO-IDF 2006 diabetes diagnostic criteria.

Generally, from the initial scoping review conducted, it was observed that there were not too major differences in these criteria, and that many epidemiological surveys after 1985 were conducted based on one or a combination of these criteria. See **Table 2.5** for more details on diabetes diagnostic criteria.

Data extraction

All extracted data were stored in 2010 Microsoft excel file format. From each selected study, data extracted included the study location and country, study period and setting, study design, diagnostic criteria. The numerical data included sample size, mean age or age range, number of diabetes, IGT or IFG cases and their respective age- and sex-specific prevalence estimates. For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were included in the selected paper.

All extracted data were sorted by country, study period, age, and their respective case numbers, sample sizes and prevalence estimates. Data were broadly grouped into mixed, rural and urban settings, and extracted figures on diabetes, IGT and IFG were separately recorded into these groups, when provided.

Data analysis

A random-effect meta-analysis was conducted on extracted crude prevalence rates of diabetes, IGT and IFG (DerSimonian and Laird, 1986). Pooled prevalence rates were further estimated for data on mixed, rural and urban settings respectively, to allow for comparisons with our modelled estimates. All estimates were reported in percentages. The rationale for using random effects meta-analysis has been earlier described. Each measure of heterogeneity and appropriateness of combining heterogeneous studies is further described under *study limitations*. The overall estimates of age- and sex-specific prevalence and incidence from all studies were used in the epidemiological modelling (**Appendix 4**). The use of age-specific estimates and mean age (and limitations) has been highlighted earlier. This is further described under *study limitations*.

Table 2.5. Diabetes diagnostic criteria

Diagnostic criteria	*Blood glucose indices*		*Glucose concentration mmol/l (mg/dl)*			
			Whole blood		**Plasma**	
			Venous	**Capillary**	**Venous**	**Capillary**
WHO 1985 (World Health Organization, 1985)	Diabetes	Fasting	≥6.7 (≥120)	≥6.7 (≥120)	≥7.8 (≥140)	≥7.8 (≥140)
		2-h PG	≥10.0 (≥180)	≥11.1 (≥200)	≥11.1 (≥200)	≥12.2 (≥220)
	IGT	Fasting	<6.7 (<120)	<6.7 (<120)	<7.8 (<140)	<7.8 (<140)
		2-h PG	6.7-10.0 (120-180)	7.8-11.1 (140-200)	7.8-11.1 (140-200)	8.9-12.2 (160-220)
ADA 1997 (Gabir et al., 2000)	Diabetes	Fasting	-	≥7.0 (≥126)	-	-
		2-h PG	-	≥11.1 (≥200)	-	-
		Casual	-	≥11.1 (≥200)	-	-
	IGT	2-h PG	-	7.8-11.1 (140-200)	-	-
	IFG	Fasting	-	6.1-6.9 (110-125)	-	
WHO 1998 (Alberti and Zimmet, 1998)	Diabetes	Fasting	≥6.1 (≥110)	≥6.1 (≥110)	≥7.0 (≥126)	-
		2-h PG	≥10.0 (≥180)	≥11.1 (≥200)	≥11.1 (≥200)	-
	IGT	Fasting	<6.1 (<110)	<6.1 (<110)	<7.0 (<126)	-
		2-h PG	6.7-10.0 (120-180)	7.8-11.1 (140-200)	7.8-11.1 (140-200)	-

	IFG	Fasting	5.6-6.1 (100-110)	5.6-6.1 (100-110)	6.1-7.0 (110-126)	-
		2-h PG	<6.7 (<120)	<7.8 (<140)	<7.8 (<140)	-
ADA 2003 (Gabir et al., 2000)	Diabetes	Fasting	-	-	≥7.0 (≥126)	-
		2-h PG	-	-	≥11.1 (≥200)	-
		Casual	-	-	≥11.1 (≥200)	-
	IGT	2-h PG	-	-	7.8-11.1 (140-200)	-
	IFG	Fasting	-	-	5.6-6.9 (100-125)	-
WHO-IDF 2006 (World Health Organization, 2006)	Diabetes Mellitus	Fasting	-	-	≥7.0 (≥126)	-
		2-h PG	-	-	≥11.1 (≥200)	-
	IGT	Fasting	-	-	<7.0 (<126)	-
		2-h PG	-	-	7.8-11.1 (140-200)	-
	IFG	Fasting	-	-	6.1-6.9 (110-126)	-
		2-h PG	-	-	<7.8 (<140)	-

Description of the modelling

For the modelling, due to more data points, and to allow for an understanding of the changing prevalence of diabetes over the last two decades, all data before 1995, from 1995 to 2004, and from 2005 to 2013 were used to estimate diabetes cases for the years 1990, 2000 and 2010, respectively.

As noted earlier, the general approach to the epidemiological modelling has already been described. In this particular model, exponential function was used for the estimation of diabetes prevalence rates and cases in Africa as it showed the greatest prediction power. The equation generated was used to determine the prevalence of diabetes in Africa at midpoints of the United Nation population 5-year age-group population estimates for Africa, for the years 1990, 2000, 2010, respectively (United Nations, 2013), see **Equation 4**. This further implies that prevalence of diabetes and corresponding cases (for the ages 15 years and above, which were predominantly the age groups from most studies) are estimated based on the UN population estimates for Africa for the ages 15-19, 20-24, 25-29, 30-34, etc, at points 17, 22, 27, 32, etc. See **Appendix 4** for all data used in modelling. All statistical analyses were conducted on 2010 Microsoft Excel and Stata 13.1 (Copyright 1985-2013 Stata Corp LP).

Equation 4

Number of diabetes cases in Africa in 2010 =
Estimated prevalence from epidemiological model * UN population for Africa in 2010 / 100

For the calculation of Confidence Interval (CI), I applied the Kirkwood and Sterne Confidence Interval for Rate (Kirkwood and Sterne, 2003), page 238, see **Equation 2.**

2.4 CANCER

Search strategy and data sources

Medical Subject Headings (MESH) and keywords were identified after initial consultations with a librarian, and a final search strategy was developed. A systematic search of Medline, EMBASE and Global Health was conducted, with publication dates set from 1980 up to December 2013. A further search was conducted on Google Scholar.

As most cancer studies were registry-based, I conducted additional searches of International Association of Cancer Registries (IACR), International Agency for Research on Cancer (IARC), and WHO African region websites to gather more data as most cancer registries send their data to these organizations. Global publications on cancer were further reviewed, including: the "GLOBOCAN studies", "Cancer Incidence in Five Continents (CI5) series", and "Cancer in Africa: Epidemiology and Prevention", and relevant publications from these studies were selected. For studies that have been identified in the databases' searches, any additional data (when available) on these studies were extracted from these global publications.

Experts on cancer research in Africa were also contacted to seek their opinion on key journals and other relevant African databases, links and websites. For identified key authors and relevant search terms, an e-mail alert was registered and new publications were automatically sent to my e-mail. Hand-searching of reference lists of all relevant publications, and key journals, were finally done to identify more studies that could have been omitted from the databases' searches. The list of African countries included in the searches was based on the World Bank list of economies (October 2013) (World Bank, 2014b). The search terms employed on Medline are shown in **Table 2.6,** while search terms for EMBASE and Global Health are shown in **Appendix 1g** and **1h**, respectively.

As noted in the introduction, the top five cancers worldwide in 2008 were lung, breast, colorectal, stomach, and liver cancer. Based on Parkin et al., the top six cancers in Africa among women were cervical cancer, breast cancer, Kaposi's

sarcoma, liver cancer, non-Hodgkin lymphoma (NHL) and ovarian cancer, and among men, these were Kaposi's sarcoma, liver cancer, prostate cancer, bladder cancer, NHL and oesophageal cancer (Parkin et al., 2008). Therefore, to have a better understanding of the cancer burden in Africa and to allow for relevant global comparisons, I limited my review to the top cancers in Africa that have contributed highly to the cancer burden in the continent, based on these previous studies. Data on cancer that were extracted and analysed therefore included top six cancers in Africa in both sexes listed above, in addition to lung, colorectal, and stomach cancers, which were the other top cancers globally, that were not listed in Africa by Parkin and colleagues (Parkin et al., 2008). Therefore, the cancer types reviewed were cervical, breast, prostate, ovary, oesophagus, bladder, Kaposi, liver, stomach, colorectal, lung and non-Hodgkin lymphoma.

Table 2.6. Search terms for studies of cancer in Africa (Medline)

#	*Searches*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp neoplasms/ or exp leukemia/ or exp lymphoma, non-hodgkin/ or exp burkitt lymphoma/ or exp sarcoma/ or exp sarcoma, kaposi/ or exp breast neoplasms/ or exp breast neoplasms, male/ or exp carcinoma, ductal, breast/ or exp "hereditary breast and ovarian cancer syndrome"/ or exp inflammatory breast neoplasms/ or exp gastrointestinal neoplasms/ or exp esophageal neoplasms/ or exp intestinal neoplasms/ or exp colorectal neoplasms/ or exp adenomatous polyposis coli/ or exp colonic neoplasms/ or exp sigmoid neoplasms/ or exp colorectal neoplasms, hereditary nonpolyposis/ or exp rectal neoplasms/ or exp anus neoplasms/ or exp ileal neoplasms/ or exp jejunal neoplasms/ or exp stomach neoplasms/ or exp liver neoplasms/ or exp adenoma, liver cell/ or exp carcinoma, hepatocellular/ or exp lung neoplasms/ or exp bronchial neoplasms/ or exp carcinoma, bronchogenic/ or exp carcinoma, non-small-cell lung/ or exp small cell lung carcinoma/ or exp pleural neoplasms/ or exp pleural effusion, malignant/ or exp solitary fibrous tumor, pleural/ or exp tracheal neoplasms/ or exp uterine neoplasms/ or exp uterine cervical neoplasms/ or exp prostatic neoplasms/ or exp kidney neoplasms/ or exp urinary bladder neoplasms/
13	1 and 11 and 12

Selection criteria

The inclusion criteria were:

i. Population-based studies (registry or cross-sectional surveys) on cancer or specific cancer types ;

ii. Studies conducted primarily on African population groups;

iii. Studies providing numerical estimates on the incidence of cancers; and

The exclusion criteria were:

i. Studies that had non-human subjects;

ii. Studies conducted before 1980; and

iii. Studies that were mainly reviews, viewpoints or editorials.

No language restrictions were applied.

Quality criteria and grading

Quality of studies was assessed based on the following criteria:

i. *Study design*: Under this, flaws in the design and execution of study were examined. As studies here were mainly registry-based, the quality checks here included active or passive cancer registration process, and cancer diagnosis and/or morphologic verification

ii. *Study analysis*: This assesses the appropriateness of statistical and analytical methods in the estimation of cancer incidence;

iii. *Study limitations*: This assesses if the study stated the limitations, as this may further guide in the choice of selection; and

iv. *Generalizability to the African population*: This broadly assesses if the study site was representative of a larger population that can be generalized to the total African population

For the quality grading, I adapted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines (Balshem et al., 2011), as follows:

i. *High quality*: Studies with the entire four criteria, or any three including "study design", highlighted above well represented;

ii. *Moderate quality*: Studies with any three of the four criteria, or any two including "study design", highlighted above well represented;

iii. *Low quality*: Studies with any two of the four criteria, or "study design" only, highlighted above well represented; and

iv. *Very low quality*: Studies with only one (excluding "study design") or none of the four criteria highlighted above well represented.

As a basic rule, all studies that were graded as *high and moderate quality* were included in the quantitative analysis. Some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, and were described further in the discussion section. However, all *very low quality* studies have been excluded from the review.

Case definitions

From the initial scoping review, it was evident that there were not many original population bases cross-sectional or cohort studies on cancers in Africa. Most of the relevant studies were mainly population-based or hospital-based registries' surveys. It was identified that the difficulties in diagnosis of cancers and lack of trained health staffs (including oncologists) in many parts of Africa have limited ongoing research efforts. This understanding ultimately shaped the scope of this systematic review on cancers in Africa.

In my search, I looked for studies that identified cancers based on doctor's diagnosis, clinical diagnosis, or laboratory (histological/cytological) diagnosis. These were not always provided due to incompleteness of many cancer registries in Africa.

Based on the above, the case definitions needed to comply with these:

i. Studies reporting diagnosis of cancer confirmed by a recognized medical practitioner, with the inclusion of terms synonymous to cancers. This include, albeit not limited to: "malignancy," "carcinoma," "sarcoma," "leukemia," and "lymphoma"; or

ii. Studies reporting laboratory-confirmed cases evident from positive histology or cytology; and/or

iii. Studies reporting compatibility with the International Classification of Diseases for Oncology (ICD-O) and/or the appropriate International Classification of Diseases (ICD) applied for analysis (World Health Organization, 1976, IARC, 1987, Percy et al., 1990)

This implies that, in these studies, incident cases of cancers have been classified according to the primary anatomic site (topography) and cellular characteristics (morphology including histology, behaviour, and grade) in accordance to ICD-O and ICD.

Data extraction

All extracted data were stored in 2010 Microsoft Excel file format.

Data was extracted systematically on study location, study period, mean age or age range, person years or sample size, incident cases of cases of cancers, and where given, the respective age-, sex- and cancer-specific incidence rates. As noted above, to ensure extracted figures from published studies were consistent all through, data on cancer incidence in Africa were further checked from websites of the WHO African Region, International Association of Cancer Registries (IACR), International Agency for Research on Cancer (IARC), and relevant publications on cancers in Africa including "GLOBOCAN studies", "Cancer Incidence in Five Continents (CI5) series" and "Cancer in Africa: Epidemiology and Prevention".

As noted in the introduction, the top five cancers worldwide in 2008 were lung, breast, colorectal, stomach, liver cancers, and based on Parkin et al, the top six cancers in Africa among women were cervical cancer, breast cancer, Kaposi's sarcoma, liver cancer, non-Hodgkin's lymphoma (NHL) and ovarian cancer, and among men, these were Kaposi's sarcoma, liver cancer, prostate cancer, bladder cancer, NHL and oesophageal cancer (Parkin et al., 2008). Therefore, to have a better understanding of the cancer burden in Africa and to allow for relevant global comparisons, the final analysis included top six cancers in Africa in both sexes, in addition to lung, colorectal, stomach cancers, which were the other top cancers

globally, that were not initially listed in Africa by Parkin and colleagues (Parkin et al., 2008).

Data analysis

As noted in the introduction, incidence rates of cancer types have been the major studies conducted in Africa, and this have mainly been based on data collated from registries. Prevalence studies on cancer are almost non-existent in Africa (African Organization for Research and Training in Cancer, 2013). Therefore, this analysis is mainly restricted to the available data, which are mainly incidence data from registry-based studies.

From extracted incidence rates of cancers in a given site, I conducted a random effect meta-analysis for specific cancers (DerSimonian and Laird, 1986), sorted according to sex, with pooled effect of cancer incidence rates expressed per 100,000 person years. All statistical analyses were conducted on Microsoft Excel and Stata 13.1 (Copyright 1985-2013 Stata Corp LP).

As many studies did not provide age group cancer incidence rates, no further modelling was conducted, as the epidemiological model earlier described is plotted along the with subjects age. Therefore, for the systematic review of cancer in Africa in this thesis, I have only provided the meta-estimate of incidence rates in the results, and the number of cases of the specific cancer was estimated from this.

2.5 CHRONIC RESPIRATORY DISEASES

2.5.1 Chronic Obstructive Pulmonary Disease (COPD)

Search strategy and databases

After an initial scoping review with further useful hints from a librarian, relevant medical subject headings (MeSH) and keywords were identified; a final search strategy was developed.

A systematic search of Medline, EMBASE and Global Health was conducted, with publication dates set from 1980 up to December 2013. A further search was conducted on Google Scholar. The list of African countries included in the searches was based on the World Bank list of economies (October 2013) (World Bank, 2014b). Experts on chronic respiratory diseases and COPD research in Africa were also contacted to seek their opinion on key journals and relevant African databases, links and websites. For identified key authors and relevant search terms, an e-mail alert was registered and new publications were automatically sent to my e-mail. Hand-searching of reference lists of relevant publications, and key journals, were finally done to identify more studies that could have been omitted from the databases' searches. The search terms employed on Medline are shown in **Table 2.7,** while search terms for EMBASE and Global Health are shown in **Appendix 1i** and **1j**, respectively.

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Table 2.7. Search terms for studies on COPD in Africa (Medline)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp Emphysema/
13	copd.mp.
14	exp bronchitis, chronic/ or exp pulmonary disease, chronic obstructive/ or exp pulmonary emphysema/
15	12 or 13 or 14
16	1 and 11 and 15

Study selection criteria

The inclusion criteria were:

i. Original population-based, cohort or cross-sectional studies on COPD and/or chronic bronchitis;

ii. Studies conducted in urban, rural, occupational, or mixed settings mainly within African population groups;

iii. Studies providing numerical estimates on the prevalence of COPD and/or chronic bronchitis; and

iv. Studies that provided clearly defined, unambiguous methodologies.

The exclusion criteria were:

i. Studies that were hospital-based;

ii. Studies that had non-human subjects;

iii. Studies conducted before 1980; and

iv. Studies that were mainly reviews, viewpoints or editorials.

Generally, no language restrictions were applied.

Quality criteria and grading

Quality of studies was assessed based on the following criteria:

i. *Study design*: Under this, flaws in the design and execution of study were examined. Basically, this assesses methods of estimation of sample size and sampling methods across studies, and the methods of dealing with design specific issues such as: training of study investigators, adherence to standardized protocol for COPD estimation by spirometry and/or symptomatic case definitions, pre-testing and reviewing questionnaires before data entry, and addressing recall and interviewer's bias appropriately;

ii. *Study analysis*: This assesses the appropriateness of statistical and analytical methods employed across studies in the estimation of the prevalence of COPD;

iii. *Study limitations*: This assesses if the study stated the limitations, as this may further guide in the choice of selection; and

iv. *Generalizability to the African population*: This broadly assesses if the study site was representative of a larger population that can be generalized to the total African population

For the quality grading, I adapted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines (Balshem et al., 2011), as follows:

i. *High quality*: Studies with the entire four criteria, or any three including "study design", highlighted above well represented;

ii. *Moderate quality*: Studies with any three of the four criteria, or any two including "study design", highlighted above well represented;

iii. *Low quality*: Studies with any two of the four criteria, or "study design" only, highlighted above well represented; and

iv. *Very low quality*: Studies with only one (excluding "study design") or none of the four criteria highlighted above well represented.

As a basic rule, all studies that were graded as *high and moderate quality* were included in the quantitative analysis. Some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, and were described further in the discussion section. However, all *very low quality* studies have been excluded from the review.

Case definitions

Primary research on COPD in Africa has been very limited. This has in part been linked to challenges in the accurate diagnosis of this condition and the heterogeneity of published research protocols (Aisanov et al., 2012). Furthermore, existing reviews have identified only ten countries in Africa that have conducted and published research findings on COPD and these are mainly from selected populations and occupational settings where the case definitions were mostly based on respiratory symptoms (Mehrotra et al., 2009, Musafiri et al., 2011a, van Gemert et al., 2011). These have all limited on-going research efforts towards determining the true burden of COPD in Africa.

Various published reports have noted that symptoms of COPD and other obstructive airway diseases do overlap, which often complicates the case ascertainment during epidemiological surveys. For example, some clinical studies show that patients with bronchial inflammation and obstruction could present with signs and symptoms of asthma, chronic bronchitis and emphysema (Musafiri et al., 2011a). In fact, COPD has previously been described in this regard, i.e. in terms of its clinical and pathological presentation, mainly as "chronic bronchitis" and "emphysema" (Menezes et al., 2004, Vijayan, 2013). The British Medical Research Council (BMRC) defines chronic bronchitis as:

> "a chronic productive cough for three months in each of two successive years in a patient in whom other causes of chronic cough have been excluded" (MRC, 1965)

And Emphysema as:

> "an abnormal and permanent enlargement of the airspaces distal to the terminal bronchioles that is accompanied by destruction of the airspace walls, without obvious fibrosis" (MRC, 1965)

These definitions, however, have not adequately explained the basic physiological impairment of the lungs in a COPD patient that, according to pulmonologists, can be traced to a reduced expiratory volume compared to the vital capacity of the lungs (Aisanov et al., 2012). As a rule, patients having chronic bronchitis, emphysema, or both may not be considered to have COPD unless there are evidences of airflow limitation (Aisanov et al., 2012, Vijayan, 2013).

Asthma is another obstructive airway disease that shares many clinical and physiologic overlaps with COPD. According to the Global Initiative for Asthma (GINA), asthma is defined as:

> "Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment" (Masoli et al., 2004)

For clinical clarifications, pulmonologists have further stated that asthma patients presenting with a completely reversible airflow obstruction may not be considered to have COPD (Masoli et al., 2004).

Meanwhile, the Global Initiative for Chronic Obstructive Lung Disease (GOLD), is a scheme introduced by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO). According to GOLD, COPD is defined as:

> "a common preventable and treatable disease, is characterized by airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients." (GOLD, 2005)

However, for the definitive evaluation and diagnosis of COPD, pulmonary function tests (PFTs), particularly spirometry, have been described as the main stay (GOLD, 2005). PFTs also further helps in determining disease severity, staging, disease progression and response to treatment (Aisanov et al., 2012). In the use of spirometry for evaluating suspected COPD cases, a pre- and post-bronchodilator is administered (e.g. inhalation of albuterol 400 µg) to help ascertain if the airflow limitation is fully or partially reversible (GOLD, 2005). The main spiromery indices employed in diagnosis are the forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC). Based on these two indices, the Global Initiative on Obstructive Lung Disease (GOLD) and the 'American Thoracic Society/ European Respiratory Society' (ATS/ERS) have provided clearer quantitative definitions of COPD, which is defined as a ratio of post bronchodilatory forced expiratory volume in one second to forced vital capacity that is less than 70% (PBD $FEV_1/FVC < 0.7$) (GOLD, 2005, Gjevre et al., 2006). While PBD $FEV_1/FVC < 0.7$ has been considered the gold standard in the diagnosis of COPD, evidences suggests that the ratio of FEV_1 to FVC

decreases with age, this may therefore need careful interpretation in older age groups (GOLD, 2005, Gjevre et al., 2006). The use of lower limit of normal (LLN) of the FEV_1/FVC has therefore been advocated in some quarters, stating that the distinction between LLN and 0.7 in older age groups may not lead to significant differences in COPD diagnosis, especially since most clinical diagnoses are usually combined with physiologic assessments (Musafiri et al., 2011b).

Based on the above understanding of COPD, in the selection of studies for the estimation of COPD in Africa, the following were considered:

i. Studies considering presence of symptoms suggestive of COPD. For example, dyspnea at rest or on exertion, cough with or without sputum production, and progressive limitation of activity

ii. Studies that employed spirometry in determining airflow limitation, mainly from $FEV_1/FVC < 0.7$ or $FEV_1/FVC <$ LLN

Therefore, based on *i* and *ii* above, the final case definitions of selected studies needed to comply with:

i. the Global Initiative on Obstructive Lung Disease (GOLD) criteria; or

ii. the American Thoracic Society/ European Respiratory Society (ATS/ERS) criteria (21);

(with GOLD and ATS/ERS criteria both broadly defined as a post-bronchodilatory (PBD) ratio of forced expiratory volume in one second to forced vital capacity of less than 70% (PBD $FEV_1/FVC < 0.7$)); or

iii. $FEV_1/FVC <$ LLN; and/or

iv. the 1965 British Medical Research Council (BMRC) definition of chronic bronchitis.

See **Table 2.8** for detailed diagnostic criteria.

Table 2.8. GOLD and ATS/ERS COPD diagnostic criteria

GOLD criteria	
Stage	***Definition***
I	$FEV_1/FVC < 0.7$; $FEV_1 \geq 80\%$ predicted
II	$FEV_1/FVC < 0.7$; FEV_1 50-80% predicted
III	$FEV_1/FVC < 0.7$; FEV_1 30-50% predicted
IV	$FEV_1/FVC < 0.7$; $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure
ATS/ERS criteria	
Severity	***Definition***
At risk Patients who: -Smoke/Pollutant exposure -Cough/Sputum/Dyspnoea -Family history of respiratory disease	Post-bronchodilator $FEV_1/FVC > 0.7$ $FEV_1 \geq 80\%$ predicted
Mild COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$; $FEV_1 \geq 80\%$ predicted
Moderate COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$; FEV_1 50-80% predicted
Severe COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$; FEV_1 30-50% predicted
Very Severe COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$; $FEV_1 < 30\%$ predicted

ATS: American Thoracic Society, ERS: European Respiratory Society, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, GOLD: Global Initiative for chronic Obstructive Lung Disease

Data extraction

Relevant data were extracted from the retained studies and saved in 2010 Microsoft Excel file format. Data extracted included corresponding country, the study period, the mean age (and any age groups that were studied specifically), the number of cases, the sample size and the prevalence of the COPD (expressed as percentages). Studies were broadly grouped into "spirometric" (defined as complying with case definitions 'i, ii and iii', as mentioned above) and "non-spirometric" (defined as complying with case definitions 'iv'). For studies conducted on the same study site, population or cohort, the first chronologically published study has been considered, with all additional new data from more recent studies further added.

Data analysis

Due to very limited data points, and heterogeneities across the few selected spirometry studies (designs, spirometry procedures, study populations clearly vary across these spirometry studies), no pooled estimate and further epidemiological modelling was conducted.

From individual studies, estimation of COPD prevalence was conducted based on spirometry or survey of obstructive airways symptoms across different population groups, ranging from a general population, occupational settings to populations involving only women. Therefore, to allow for an understanding of the prevalence of COPD across these populations, the prevalence of COPD was separately investigated from "spirometric" and "non-spirometric" sets of studies and the effect of covariates (e.g., mean age, gender, the year of study and the country) were analysed. I therefore generated box plots of spirometric and non-spirometric prevalence based on gender, and also generated scatter plots of spirometric and non-spirometric prevalence based on mean age. The prevalence of COPD from the two types of studies ("spirometric" and "non-spirometric") was then compared. In addition, Pearson correlation coefficients, t-test on equality of means, and Mann-Whitney test for equality of medians were used to study the effects of case definition and other covariates on the prevalence of COPD.

Finally, as I could not generate pooled or modelled estimates (and confidence intervals) from these datasets, I applied the median and inter-quartile prevalence

range from spirometry-based studies, which is the gold-standard diagnostic procedure for COPD, and the United Nation (UN) Population Division's population figures (United Nations, 2013), to estimate the number of COPD cases in the year 2010, see **Equation 5**. All statistical analyses were conducted on 2010 Microsoft Excel, SPSS and Stata 13.1 (Copyright 1985-2013 Stata Corp LP).

Equation 5

Number of COPD cases in Africa in 2010 =

Median prevalence * UN population for Africa in 2010 / 100

2.5.2 Asthma

Search strategy and data sources

After an initial consultation with a librarian, relevant medical subject headings (MeSH) and keywords were identified, and a final search strategy was developed.

A systematic search of Medline, EMBASE and Global Health was conducted, with publication dates set from 1980 up to December 2013. A further search was conducted on Google Scholar. The list of African countries included in the searches was based on the World Bank list of economies (October 2013) (World Bank, 2014b). Experts on chronic respiratory diseases and asthma research in Africa were also contacted to seek their opinion on key journals and relevant African databases, links and websites. For identified key authors and relevant search terms, an e-mail alert was registered and new publications were automatically sent to my e-mail. Hand-searching of reference lists of relevant publications, and key journals, were finally done to identify more studies that could have been omitted from the databases' searches. The search terms employed on Medline are shown in **Table 2.9,** while search terms for EMBASE and Global Health are shown in **Appendix 1k** and **1l**, respectively.

Table 2.9. Search terms of studies on asthma in Africa (Medline)

#	***Searches***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp asthma/ or exp asthma, aspirin-induced/ or exp asthma, exercise-induced/ or exp asthma, occupational/ or exp status asthmaticus/ or wheezing/
13	1 and 11 and 12

Study selection criteria

The inclusion criteria were:

i. Original population-based, cohort or cross-sectional studies on asthma;
ii. Studies conducted in urban, rural, occupational, or mixed settings mainly within African population groups;
iii. Studies providing numerical estimates on the prevalence of asthma; and
iv. Studies that provided clearly defined, unambiguous methodologies.

The exclusion criteria were:

i. Studies that were hospital-based;
ii. Studies that had non-human subjects;
iii. Studies conducted before 1980; and
iv. Studies that were mainly reviews, viewpoints or editorials.

No language restrictions were applied.

Quality criteria and grading

Quality of studies was assessed based on the following criteria:

i. *Study design*: Under this, flaws in the design and execution of study were examined. Basically, this assesses methods of estimation of sample size and sampling methods across studies, and the methods of dealing with design specific issues such as: training of study investigators, adherence to standardized protocol for asthma diagnosis by spirometry and/or symptomatic case definitions, pre-testing and reviewing questionnaires before data entry, and addressing recall and interviewer's bias appropriately;

ii. *Study analysis*: This assesses the appropriateness of statistical and analytical methods employed across studies in the estimation of the prevalence of asthma;

iii. *Study limitations*: This assesses if the study stated the limitations, as this may further guide in the choice of selection; and

iv. *Generalizability to the African population*: This broadly assesses if the study site was representative of a larger population that can be generalized to the total African population

For the quality grading, I adapted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines (Balshem et al., 2011), as follows:

i. *High quality*: Studies with the entire four criteria, or any three including "study design", highlighted above well represented;

ii. *Moderate quality*: Studies with any three of the four criteria, or any two including "study design", highlighted above well represented;

iii. *Low quality*: Studies with any two of the four criteria, or "study design" only, highlighted above well represented; and

iv. *Very low quality*: Studies with only one (excluding "study design") or none of the four criteria highlighted above well represented.

As a basic rule, all studies that were graded as *high and moderate quality* were included in the quantitative analysis. Some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, and were described further in the discussion section. However, all *very low quality* studies have been excluded from the review.

Case definitions

As noted in the introduction, defining asthma has posed huge challenge to researchers, and this often has affected the conduct of epidemiological surveys, especially in Africa, where health workers have not been trained, or exposed to standard equipment needed for the diagnosis of asthma (Reddel et al., 2009). Realistically, experts have stated there is really no straight forward definition of asthma, as most surveys diagnostic criteria are based on respiratory symptoms, experience in the management of asthma, and doctors' diagnosis (Gjevre et al., 2006, Bousquet et al., 2010). One interesting way to improved identification of asthma in the community could be focusing more on survey of incident cases rather than prevalent cases of asthma, respectively (Reddel et al., 2009, Trepka et al., 2009). This offers the researcher to ask questions on recent episodes of asthma, emerging etiologic and risk factors could be more appreciated, and the health system may be prompted towards establishing asthma surveillance, notification and registration

system that can subsequently help in asthma diagnosis during future prevalence studies, as the case in the United States (Trepka et al., 2009).

According to GINA, asthma is defined as:

> "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment" (Masoli et al., 2004)

For ease of diagnosis, GINA proposed a holistic approach involving detailed history, physical examination and spirometry. An increase in FEV_1 of ≥12% and ≥200ml after a bronchodilator is indicative of reversible airflow limitation, which is consistent with asthma (Masoli et al., 2004). Other diagnostic methods that may be indicative of asthma include peak expiratory flow (PEF) with an improvement of 60l/min (or ≥20% of the pre-bronchodilator PEF) after a bronchodilator, or a diurnal variation in PEF of more than 20% (with twice daily readings more than 10%) (Masoli et al., 2004, Gjevre et al., 2006). Other non-specific diagnostic tests include methacholine or histamine test, inhaled mannitol or exercise challenge, skin prick test and measurement of serum IgE (Gjevre et al., 2006).

In this review and based on the understanding of the variations and challenges in the diagnosis of asthma, studies based on respiratory symptoms suggestive of asthma (as described by GINA) were finally included. However, it is important to note that these symptoms were mainly surveyed for across retained studies based on the written questionnaires (mainly conducted among adolescents and adults) or video questionnaires (usually conducted among children), which were initially proposed by the ISAAC study groups (Zar et al., 2007). See **Table 2.10** for further details on asthma terms and definitions.

Diagnostic criteria therefore needed to comply with:

i. Studies based on symptoms of asthma as described by GINA, e.g wheeze at rest, wheeze on exercise, nocturnal wheeze, nocturnal cough, or severe wheeze ; and/or

ii. Studies based on doctor or self-reported diagnosis of asthma

Table 2.10. Asthma symptoms and related definitions

Terms	*Definition*
Wheeze	A high pitched whistling sound originating from obstructed airways (IUATLD, 2011). "Wheeze at rest-12 months" refers to the prevalence of wheeze in a person in the last 12 months (IUATLD, 2011)
Asthma	A chronic airway disease characterized by wheezing (a high pitched whistling sound originating from obstructed airways). Patient usually present with chronic airways inflammation, bronchial hyper-responsiveness and reversible airflow obstruction, resulting in the recurrent attacks of wheeze, chest tightness, breathlessness, and occasionally cough and sputum production, all of varying severity and frequency from person to person (Masoli et al., 2004). Asthma ever refers to cummulative prevalence of asthma in a person (IUATLD, 2011)
Asthma exacerbation	Also known as acute asthma. A sudden progressive episodes of shortness of breath, usually characterized by chest tightness, wheezing, cough or sputum production (Reddel et al., 2009)
Moderate asthma exacerbation	An event that, when recognized, should result in a temporary change in treatment, in an effort to prevent the exacerbation from being severe (Reddel et al., 2009)
Severe asthma exacerbation	Events that require urgent action on the part of the patient and physician to prevent a serious outcome, such as hospitalization or death (Reddel et al., 2009)
Severe asthma	Uncontrolled asthma which can result in risk of frequent severe exacerbations (or death), and/or adverse reactions to medications, and/or chronic morbidity, including impaired lung function or reduced lung growth in children (Reddel et al., 2009)
Asthma control	Extent to which the various manifestation of asthma are reduced or removed by treatment (Reddel et al., 2009)

FEV1: forced expiratory volume in one second, GINA: Global Initiative for Asthma, IgE: immunoglobulin E, PEF: peak expiratory flow

Data extraction

Relevant data were extracted from retained studies and saved in 2010 Microsoft Excel file-format. All extracted data were sorted by country, study period, age, and their respective case number, sample size and prevalence estimate (expressed as percentages). Extracts were grouped into data from written questionnaires or video questionnaires, both including data based on doctor or self-reported asthma diagnosis, and/or its symptoms (wheeze at rest, wheeze on exercise, nocturnal wheeze, nocturnal cough, or severe wheeze). For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, with all additional data from other studies added to that of the selected paper.

Data Analysis

As noted in the introduction, asthma diagnosis based on doctor or self-reported diagnosis of asthma (asthma ever or cumulative lifetime asthma prevalence) and the symptom "current wheeze" (wheeze at rest- 12 months) have mostly been used across many studies (Yemaneberhan et al., 1997, IUATLD, 2011). Therefore, in the analysis, and to allow for a comparison with the modelled estimates, random effect meta-analysis was conducted on crude prevalence rates of asthma estimated from doctor or self-reported diagnosis of asthma (asthma ever), and symptoms (wheeze at rest, wheeze on exercise, nocturnal wheeze, nocturnal cough, or severe wheeze) (DerSimonian and Laird, 1986). These were mainly from studies based on written questionnaire, as these provided more data points that can allow for detailed analysis. Furthermore, due to more data points in the written questionnaires among urban and rural dwellers, pooled prevalence estimates of "asthma ever" and "current wheeze" were further calculated in these population sub-groups. The rationale for using random effects meta-analysis has been earlier described. Each measure of heterogeneity and appropriateness of combining heterogeneous studies is further described under *study limitations*. The overall estimates of age- and sex-specific prevalence and incidence from all studies were used in the epidemiological modelling (**Appendix 5**). The use of age-specific estimates and mean age (and limitations) has been highlighted earlier. This is further described under *study limitations.*

However, in line with reports suggesting that asthma prevalence estimates based on "current wheeze" (wheeze at rest- 12 months) provided higher sensitivities and specificities for asthma diagnosis during epidemiological surveys (IUATLD, 2011), extracted crude prevalence rates from studies based on this was employed in the overall modelling.

Description of the Modelling

Just as noted in previous sections, the general approach to the epidemiological modelling has already been described. In this particular model, polynomial function was used for the estimation of asthma prevalence rates and cases in Africa as it showed the greatest prediction power. The model was applied on all data points reporting crude prevalence of asthma based on the symptom "current wheeze" (wheeze at rest- 12 months), which has been shown to have highest sensitivity in the estimation of asthma prevalence in the population (IUATLD, 2011). The equation generated was used to determine the prevalence of asthma in Africa at midpoints of the United Nation population 5-year age-group population estimates for Africa, for the year 2010 (United Nations, 2013), see **Equation 6**. This implies that prevalence of asthma and corresponding cases are estimated based on the 2010 UN population estimates for Africa for the ages 0-4, 5-9, 10-14, 15-19, etc, at points 2, 7, 12, 17, etc. See **Appendix 5** for all data used in modelling. All statistical analyses were conducted on 2010 Microsoft Excel and Stata 13.1 (Copyright 1985-2013 Stata Corp LP).

Equation 6

Number of asthma cases in Africa in 2010 =

Estimated prevalence from epidemiological model * UN population for Africa in 2010 / 100

For the calculation of Confidence Interval (CI), I applied the Kirkwood and Sterne Confidence Interval for Rate (Kirkwood and Sterne, 2003), page 238, see **Equation 2.**

3 RESULTS

3.1 OVERVIEW

This part of the thesis also follows the same pattern presented in the methods. For each of the diseases under review (cardiovascular diseases (hypertension and stroke), diabetes, cancer, and chronic respiratory disease (COPD and asthma)), I have presented the results of the systematic review, study characteristics, pooled prevalence or incidence estimates, and modelled prevalence or incidence estimates, where there are enough data available to allow for this.

3.2 CARDIOVASCULAR DISEASES

3.2.1 Hypertension

Systematic Review

The search returned 7680 publications: 2205 in Medline, 4073 in EMBASE, and 1402 in Global Health. An additional 3 studies were included from other sources (Google Scholar and reference list of relevant reviews). After excluding duplicates, 5227 studies remained. On screening titles for relevance (hypertension studies conducted primarily in an African population setting), 4936 articles were excluded, giving a total of 291 full texts that were assessed. 82 articles did not report hypertension prevalence or population denominators from which prevalence rates can be calculated, 75 articles did not specify study designs and / or clarify case definitions of hypertension, and 42 articles were based on blood pressures base-line of 160/90mmHg. A total of 92 studies were finally retained for qualitative synthesis and quantitative analysis (**Figure 3.1**)

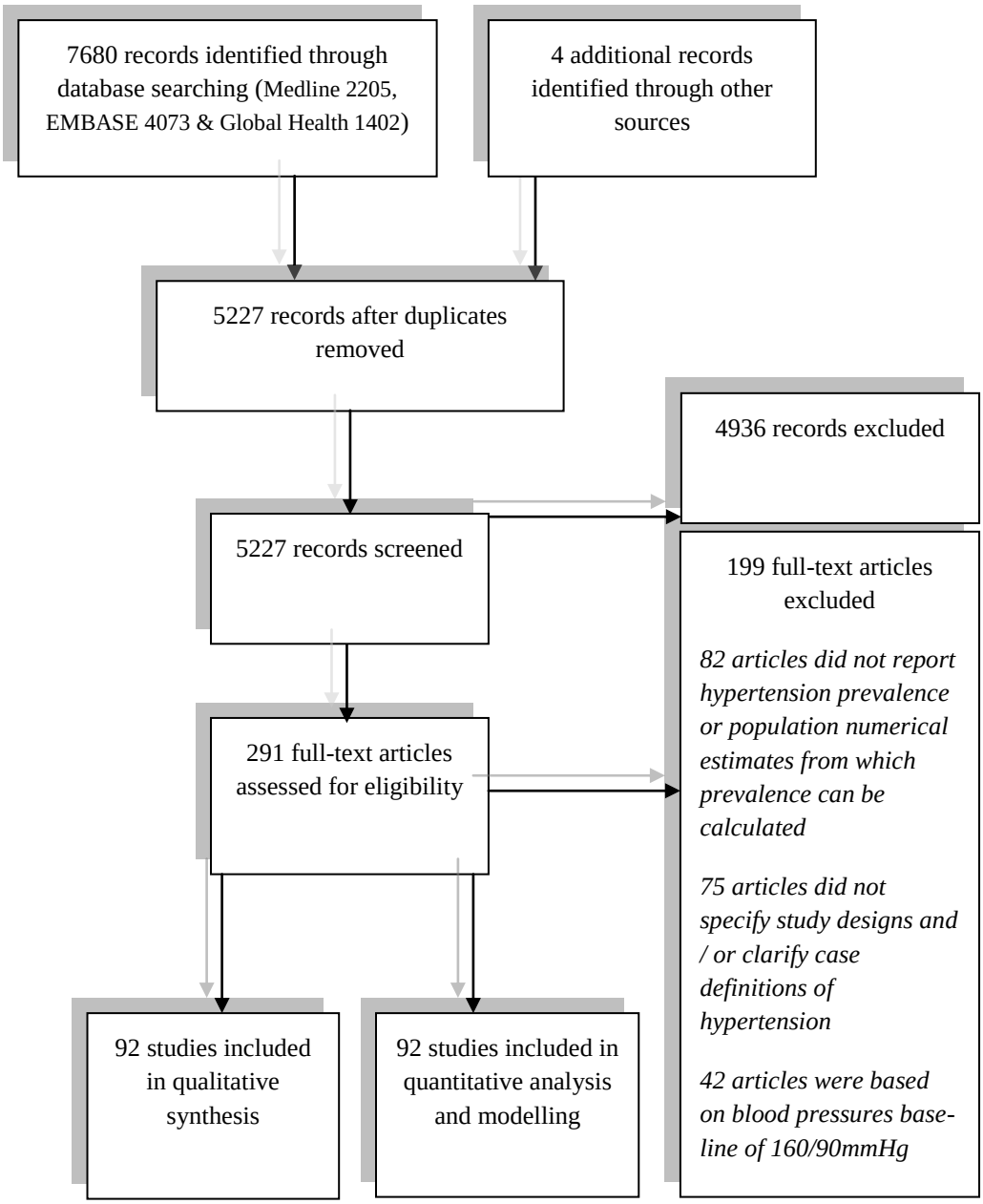

Figure 3.1. Flow diagram of search results for hypertension studies in Africa

Study characteristics

There were 92 studies conducted across 101 study sites in 31 African countries. Central Africa had 10 study sites, Eastern Africa 21, Northern Africa 12, Southern Africa 15, and Western Africa 43. Nigeria had the highest number of publications with 26 study sites; Ghana and South Africa followed with 7 study sites each, while Cameroon, Tanzania and Tunisia had 6 study sites each (see **Table 3.1** and **Figure 3.2** for details).

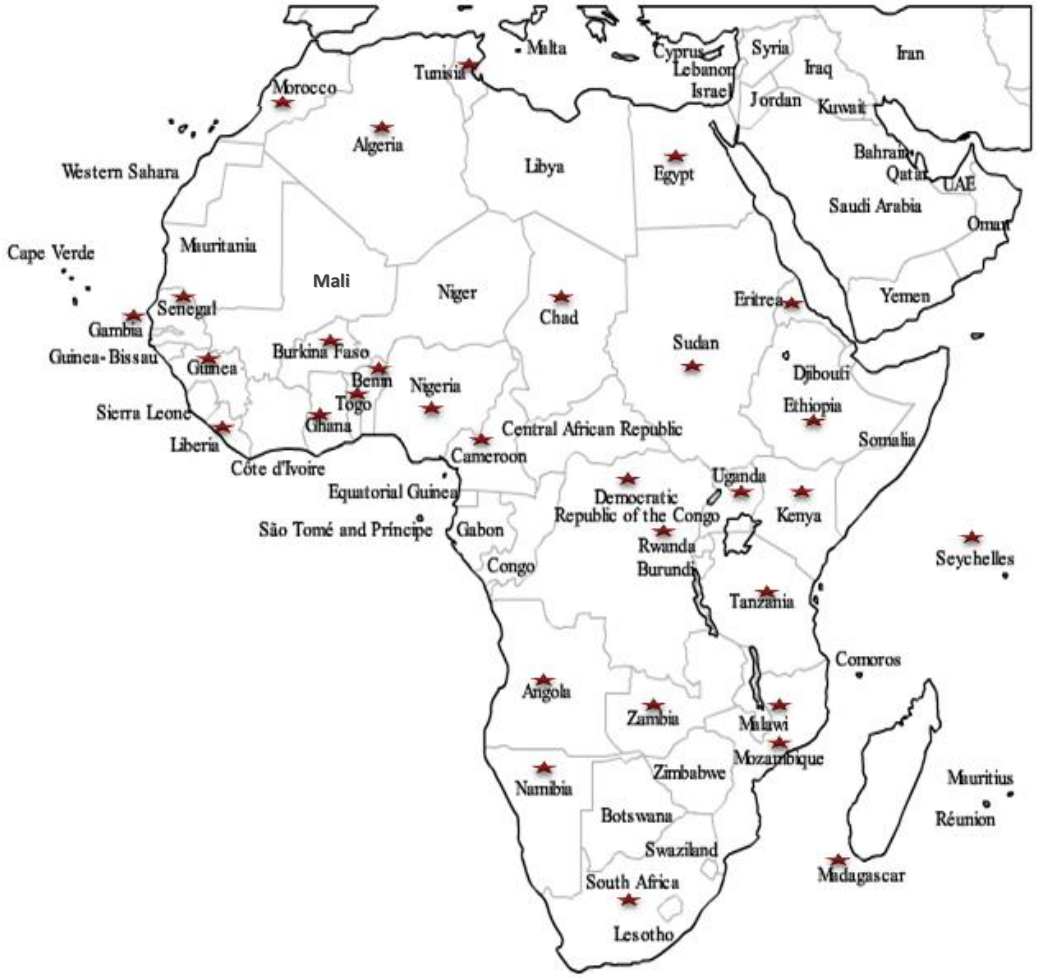

Figure 3.2. Map of Africa with asterisks showing countries of the retained hypertension studies

Table 3.1. Characteristic distribution of retained hypertension studies in Africa

Characteristics	***Country***	***Study sites***
Central Africa (10 study sites)	Cameroon	6
	Chad	1
	DR Congo	2
	Rwanda	1
Eastern Africa (21 study sites)	Eritrea	1
	Ethiopia	5
	Kenya	3
	Seychelles	1
	Sudan	1
	Tanzania	6
	Uganda	4
Northern Africa (12 study sites)	Algeria	3
	Egypt	2
	Morocco	1
	Tunisia	6
Southern Africa (15 study sites)	Angola	2
	Madagascar	1
	Malawi	2
	Mozambique	1
	Namibia	1
	South Africa	7
	Zambia	1
Western Africa (43 study sites)	Benin	1
	Burkina Faso	1
	Gambia	1
	Ghana	7

	Guinea	2
	Liberia	1
	Nigeria	26
	Senegal	2
	Togo	2
Duration of study		
<1 year		74
1-3 years		22
>3 years		5
Sample size		
<1000		54
1001-3000		37
>3000		10
Study setting		
Rural		47
Urban		50
Mixed*		33

**sites overlap with urban and rural settings*

73% of studies were completed within a one year, with over 50% carried out in urban settings. The overall sample size from all retained studies was 197,734, with a mean and median of 1958 and 1200 respectively. For the diagnosis of hypertension, retained studies were restricted to the inclusion criteria, i.e. studies based on the cut-off "≥140/90 mm Hg" (see **Tables 3.1** and **3.2)**. From all studies, the weighted mean systolic and diastolic blood pressures were 129.6 mm Hg and 78.0 mm Hg respectively. Studies were mostly conducted on people aged ≥20 years, with an estimated overall mean age of 47.4 years. For the age determination of subjects across selected studies, birth certificates were mostly employed, and in the absence of valid age-verification documents, subjects' age were determined from historical landmarks.

Table 3.2. Overall summary of data (by site) from retained hypertension studies in Africa

African region	*Country, Setting*	*Year*	*Age (years)*	*Prevalence %*		
				All	*Men*	*Female*
Central	1) Cameroon, Mixed (Cooper et al., 1997)	1995	49.5	16.9	17.7	16.3
	2) Cameroon, Mixed (Cruickshank et al., 2001)	1991	41.75	7.07	8.92	5.69
	3) Cameroon, Mixed (Fezeu et al., 2010)	1994	54.5	18.8	20.2	17.8
	4) Cameroon, Mixed (Fezeu et al., 2010)	2003	54.5	38.34	40.9	36.5
	5) Cameroon, Urban (Kamadjeu et al., 2006)	2003	31.35	24.6	25.6	23.1
	6) Cameroon, Urban (Kamadjeu et al., 2006)	2004	31.35	20.8	-	-
	7) Chad, Rural (Dionadji et al., 2010)	2004	35	16.4	12.2	21.8
	8) DR Congo, Mixed (Katchunga et al., 2011)	2009-10	54.5	40.2	-	-
	9) DR Congo (M'Buyamba-Kabangu et al., 1986)	1983-84	42.5	16.7	22.1	12.4
	10) Rwanda, Rural (de Ramirez et al., 2010)	2007	42.2	16.0	16.0	16.0
East	11) Eritea, Mixed (Mufunda et al., 2006c)	2004	39.5	16.0	16.88	15.28
	12) Ethiopia, Mixed (Giday and Tadesse, 2011)	2008	36.08	9.9	-	-
	13) Ethiopia, Urban (Awoke et al., 2012)	2012	51.4	28.3	26	30.3
	14) Ethiopia, Urban (Nshisso et al., 2012)	2009	50.5	19.1	22	14.9
	15) Ethiopia, Urban (Tesfaye et al., 2009)	2006	49.5	30.0	31.5	28.9
	16) Ethiopia, Urban (Tran et al., 2011)	2009-2010	42.9	17.7	20.0	14.3
	17) Kenya, Rural (Hendriks et al., 2012)	2009-11	40.9	20.2	-	-
	18) Kenya, Mixed (Mathenge et al., 2010)	2007-08	69.5	50.1	-	-
	19) Kenya, Urban (Van De Vijver et al., 2013)	2009-09	48.5	12.3	12.7	12
	20) Seychelles, Mixed (Bovet et al., 2006)	2004	44.5	31.6	38.4	24.8
	21) Sudan, Urban (Ahmed, 1990)	1988-89	35	7.5	-	-
	22) Tanzania, Urban (Bovet et al., 2002)	1998-99	54.5	28.9	27.1	30.2
	23) Tanzania, Rural (de Ramirez et al., 2010)	2007	42.8	27	28	24

	24) Tanzania, Rural (Dewhurst et al., 2013b)	2009-2010	76	69.9	62.2	75.8
	25) Tanzania, Rural (Edwards et al., 2000)	1996	39.95	29.2	30	28.6
	26) Tanzania, Rural (Edwards et al., 2000)	1996	54.5	31.9	32.2	31.5
	27) Tanzania, Urban (Hendriks et al., 2012)	2009-11	36.8	19	-	-
	28) Uganda, Rural (Maher et al., 2011a)	2008-09	32.75	22.3	22.5	22.6
	29) Uganda, Rural (Mayega et al., 2012)	2011	42.5	20.5	20.7	20.4
	30) Uganda (Musinguzi and Nuwaha, 2013)	2012	35.15	21.8	22.3	21.7
	31) Uganda, Rural (Wamala et al., 2009)	2006	42	30.4	25.4	34
North	32) Algeria, Rural) (Hamida et al., 2013)	2010	58.5	50.2	51.3	49.7
	33) Algeria, Urban (Latifa and Kaouel, 2007)	2004-05	54.5	32.7	24.5	40.6
	34) Algeria, Peri-urban (Temmar et al., 2007)	2006-07	55	44	41.2	46.7
	35) Egypt, Mixed (Ibrahim et al., 1995)	1991-93	45.6	26.3	25.7	26.9
	36) Egypt, Rural (Mohamed et al., 2000)	1999-00	42.5	27.9	-	-
	37) Morocco, Mixed (Tazi et al., 2003)	2000	51	39.6	37.2	41.3
	38) Tunisia, Mixed (Allal-Elasmi et al., 2012)	2004-05	44.6	31.07	25.0	36.1
	39) Tunisia, Mixed (Ben Romdhane et al., 2012)	2004-05	49.6	30.6	27.3	33.1
	40) Tunisia, Mixed (Ben Romdhane et al., 2005)	2002-03	54.5	44.3	38.7	48.2
	41) Tunisia, Urban (Ghannem and Fredj, 1997)	1995	54.5	28.9	30	28.4
	42) Tunisia, Rural (Hammami et al., 2011)	2008-09	72.3	52	45	55.5-
	43) Tunisia, Mixed (Laouani Kechrid et al., 2004)	2002-03	69	69.3	-	-
South	44) Angola, Urban (Capingana et al., 2013)	2009-10	44.5	45.2	46.3	44.2
	45) Angola, Mixed (Pires et al., 2013)	2011	41.5	23	26.4	19.8
	46) Madagascar, Urban (Mauny et al., 2003)	1996-97	32.75	23.3	24.9	21.7
	47) Malawi, Rural (de Ramirez et al., 2010)	2007	38.4	23	24.5	22
	48) Malawi, Mixed (Msyamboza et al., 2012)	2009	45.5	33.2	36.9	29.9
	49) Mozambique, Mixed (Damasceno et al., 2009)	2005	54.5	33.1	35.7	31.2
	50) Namibia, Urban (Hendriks et al., 2012)	2009-11	36.9	32	-	-
	51) South Africa, Rural (Alberts et al., 2005)	2004-05	59.5	28.0	24.5	29.2

	52) South Africa, Rural (Malaza et al., 2012)	2010	54.5	26.2	20.8	28.5
	53) S/Africa (Peltzer and Phaswana-Mafuya, 2013)	2008	65	77.3	74.4	79.6
	54) South Africa, Mixed (Steyn et al., 1986)	1982	41	41.6	45.6	37.75
	55) South Africa, Mixed (Steyn et al., 1996)	1990	40.5	21.5	19.2	23.4
	56) South Africa, Peri-urban (Steyn et al., 2004)	1996	42	27.1	31.9	23.4
	57) South Africa, Rural (Thorogood et al., 2007)	2002	59.5	32.6	-	-
	58) Zambia, Urban (Goma et al., 2011)	2009-10	57	34.8	38	33.3
West	59) Benin, Mixed (Houinato et al., 2012)	2008	42.7	27.9	-	-
	60) Burkina Faso, Urban (Niakara et al., 2007)	2004	54.5	40.2	-	-
	61) Gambia, Mixed (van der Sande et al., 2000)	1998-99	43.7	18.4	-	-
	62) Ghana, Rural (Addo et al., 2006)	2004-05	42.4	25.4	24.1	25.9
	63) Ghana, Mixed (Agyemang, 2006)	2004	35.9	29.4	31.04	28.07
	64) Ghana, Rural (Burket, 2006)	2003	53	32.8	-	-
	65) Ghana, Mixed (Cappuccio et al., 2004)	2001	54.7	28.7	29.9	28
	66) Ghana, Rural (Cook-Huynh et al., 2012)	2006-07	53.5	35	37.2	34.1
	67) Ghana, Rural (Koopman et al., 2012)	2002-10	66	24.1	25.7	22.5
	68) Ghana, Rural (Williams et al., 2013)	2012	53.84	44.7	-	-
	69) Guinea, Mixed (Balde et al., 2006)	2003	62	31.4	-	-
	70) Guinea, Rural (N'Gouin-Claih et al., 2003)	2001	45.5	45.2	-	-
	71) Liberia, Rural (Giles et al., 1994)	1991-92	54.5	12.5	-	-
	72) Nigeria, Mixed (Abegunde and Owoaje, 2013)	2010-11	71.1	34.7	-	-
	73) Nigeria, Semi-urban (Adedoyin et al., 2008)	2007-08	44.2	36.57	36.79	36.39
	74) Nigeria, Semi-urban (Adedoyin et al., 2012)	2011-12	41.5	25.2	24.7	24.7
	75) Nigeria, Rural (Ahaneku et al., 2011)	2010-11	57.3	44.5	49.3	42.3
	76) Nigeria, Rural (Alikor et al., 2013)	2012-13	41.3	20.2	20.5	20.1
	77) Nigeria, Urban (Amira et al., 2012)	2006-10	41.9	33	38.3	27.8
	78) Nigeria, Mixed (Amole et al., 2011)	2008	48.7	50.5	52	49.3
	79) Nigeria, Rural (Asekun-Olarinmoye et al., 2013)	2011	49.7	13.2	15	11.9

	80) Nigeria, Urban (Bunker et al., 1992)	1987-88	36.35	31.1	34	17
	81) Nigeria, Mixed (Cooper et al., 1997)	1995	49.5	14.5	14.7	14.3
	82) Nigeria, Rural (Ejim et al., 2011)	2005-06	59.8	46.4	50.2	44.8
	83) Nigeria, Semi-urban (Ekanem et al., 2013)	2012	31.7	47	30.1	16.8
	84) Nigeria, Mixed (Ekwunife et al., 2010)	2009	34.9	21.1	-	-
	85) Nigeria, Semi-urban (Erhun et al., 2005)	2002-03	55	21	23.3	16.4
	86) Nigeria, Rural (Hendriks et al., 2012)	2009-11	45.3	21	-	-
	87) Nigeria, Mixed (Isezuo et al., 2011)	2009-10	38.9	24.8	25.9	23.6
	88) Nigeria, Semi-urban (Mbah et al., 2013)	2011-12	50	32.5	-	-
	89) Nigeria, Urban (Odugbemi et al., 2012)	2009-10	43.88	34.8	-	-
	90) Nigeria, Mixed (Ogah et al., 2013)	2011-12	41.7	31.8	33.5	30.5
	91) Nigeria, Urban (Oghagbon et al., 2008)	2006-07	50.5	27.1	28.4	22.9
	92) Nigeria, Rural (Oladapo et al., 2010)	2002-05	42.1	20.8	21.1	20.5
	93) Nigeria, Urban) (Omorogiuwa et al., 2009)	2007-08	41.6	33	28.1	36.4
	94) Nigeria, Rural (Omuemu et al., 2007)	2004-05	30.7	20.2	24.8	13.2
	95) Nigeria, Semi-urban (Suleiman et al., 2013)	2011	50.5	15	18.8	12.5
	96) Nigeria, Mixed (Ulasi et al., 2010)	2007-08	40.8	32.8	-	-
	97) Nigeria, Mixed (Ulasi et al., 2011)	2009-10	38.02	42.2	46.3	37.7
	98) Senegal, Urban (Astagneau et al., 1992)	1989-90	31.45	22.5	23.6	21.5
	99) Senegal, Urban (Macia et al., 2012)	2009	69.5	65.4	63.9	67.1
	100) Togo, Urban (Baragou et al., 2012)	2009-10	39	26.6	25.7	27.6
	101) Togo, Urban (Yayehd et al., 2013)	2011	40.8	36.7	34.6	38.4

JNC: Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure, WHO/ISH : World Health Organization/ International Society of Hypertension

Details of quality criteria and grading of retained hypertension studies in Africa

Of the selected 92 studies, there were 5 low quality studies (**Table 3.3**). As noted in the methods, these low quality studies were included in the meta-analysis and modelling due to the well explained study designs, and because their exclusion do not provide any significant change in the overall pooled prevalence of hypertension.

Table 3.3. Quality assessment of retained hypertension studies in Africa

Study ID*	***Study design***	***Study analysis***	***Study limitations***	***Generalizability to Africa***	***Grading***
1-4, 7, 10, 11, 13-16, 18-20, 22-26, 28-35, 37-41, 44-49, 51, 52, 57, 58, 60, 62, 63, 65-68, 72-77, 79-87, 90-95, 97-101	Well explained, excluding 46 and 68 (where training/questionnaire pre-test were not clearly stated)	Well explained, excluding 60	Well-presented across all studies	Study population representative of a larger African population across all studies	*High*
5, 6, 9, 12, 17, 21, 27, 36, 42, 43, 50, 53, 59, 64, 69, 70, 78, 88, 89, 96	Well explained, excluding 21, 64, and 78 (where there was no clear description of population survey)	Well explained, excluding 5, 6, 17, 36, 42, 50, 53, 88 and 96	Well-presented excluding 9, 12, 27, 43, 59, 69, 70, 89	Study population not representative of a larger African population, excluding 21, 64 and 78 that were based on elderly population groups	*Moderate*
8, 54, 56, 60, 71	Well explained	Not well explained	Not well presented	Study population not fairly representative of a larger African population	*Low*

see **Table 3.2 for details of Study ID*

Hypertension prevalence distribution in individual studies

Across all study settings, an elderly South African site recorded the highest prevalence of hypertension in 2008 (77.3%, mean age 65 years) (Peltzer and Phaswana-Mafuya, 2013). Other settings reporting higher prevalence rates of hypertension were also in older adult population surveys in Tanzania in 2010 (69.9%, mean age 76 years), Tunisia in 2003 (69.3%, mean age 69 years), and Senegal in 2009 (65.4%, mean age 69.5 years) respectively (Dewhurst et al., 2013b, Laouani Kechrid et al., 2004, Macia et al., 2012). The lowest prevalence rates of hypertension were recorded in Sudan (7.5%, mean age 35 years) and Ethiopia (9.9%, mean age 36.1 years) in 1989 and 2008 respectively (Ahmed, 1990, Giday and Tadesse, 2011) (See **Table 3.2** for overall study characteristics).

Overall pooled prevalence of hypertension in Africa

The overall pooled crude prevalence of hypertension for Africa was:

i. 20.5% (95%CI: 14.4-26.6, I^2=99.3, p=0.000), males 23.0%, females 20.2% in 1990;

ii. 31.0% (95%CI: 26.8-35.3, I^2=98.9, p=0.000), males 26.9, females 28.4 in 2000; and

iii. 31.9 (95%CI: 28.6-35.3, I^2=99.5, p=0.000), males 29.7%, females 31.4% in 2010.

Further analysis by study settings did not reveal a large difference in hypertension prevalence between urban and rural dwellers. In 2000 and 2010, urban and rural dwellers had a prevalence of 26.1% versus 26.3%, and 29.6% versus 29.0%, respectively. However, in 1990, urban dwellers recorded a prevalence of 17.2% (males 21.1%, females 15.1%), compared to 11.1% (males 9.4%, females 8.3%) recorded among rural dwellers (see **Table 3.4** for details).

Pooled prevalence of hypertension in African sub-regions

The pooled crude prevalence in Northern Africa was higher than in sub-Saharan Africa (SSA), with hypertension prevalence of 33.3% in Northern Africa and 27.8% in sub-Saharan Africa. In other parts of SSA, Southern Africa recorded the highest prevalence, with a prevalence of 34.6% (males 35.4%, females 34.2%). Western Africa had a prevalence of 27.3% (males 29.6, females 28.2), Central Africa recorded 21.1% (males 21.5%, females 19.3%), and Eastern Africa had 26.8% (males 25.0, females 26.1) (see **Table 3.5** for details).

Awareness rate of hypertension in Africa

Generally, across studies, participants with hypertension were considered aware of their condition if they responded "yes" to the question "Have you ever been told by a doctor or certified health care professional that you had hypertension?"

Across selected studies, there is evidence suggesting the awareness of hypertension among people living with the disease has been increasing since 1990; however, the overall awareness rate still remains relatively low in many parts of Africa. From the analysis, pooled awareness rate (expressed as a percentage of the cases of hypertension) of 16.9% was estimated in 1990, 29.2% in 2000 and 33.7% in 2010 (see **Table 3.4**). However, from the regional awareness rate of hypertension, Eastern Africa had the highest pooled awareness rate at 40.9%, followed by Northern Africa with an awareness rate of 36.2%, Southern Africa 26.4%, Central Africa 25.1%, and Western Africa 21.7% (see **Table 3.5**).

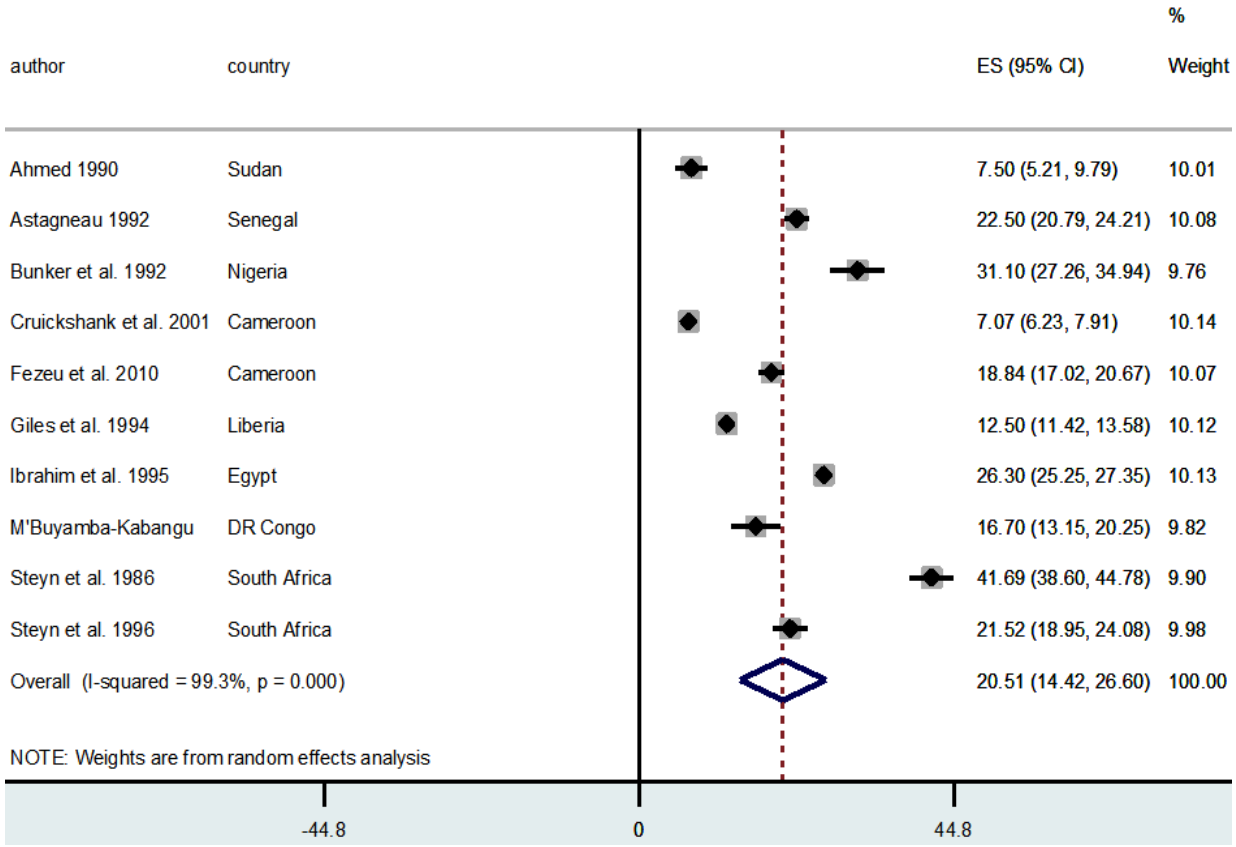

Figure 3.3. Forest plot showing overall pooled hypertension prevalence in Africa in 1990

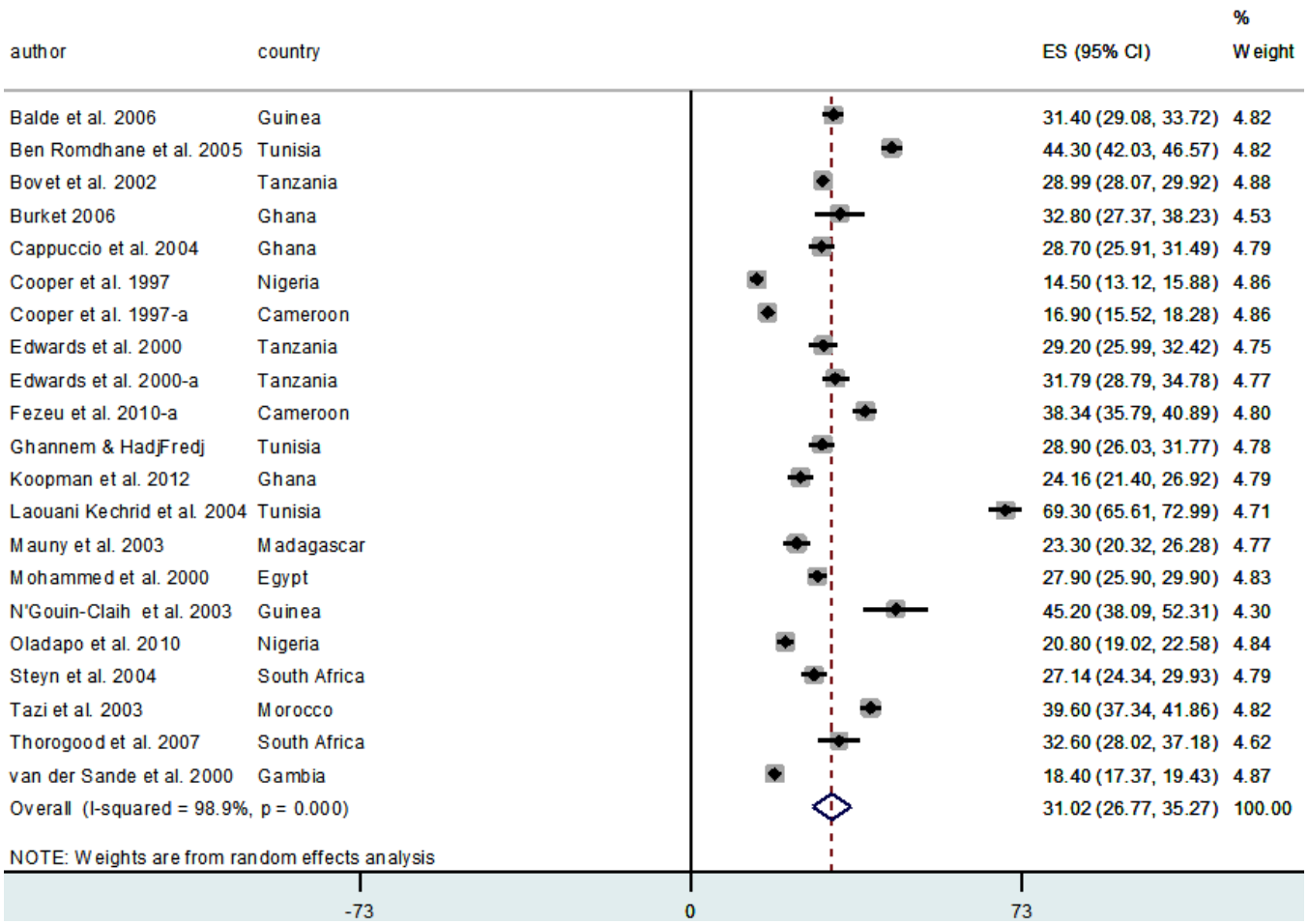

Figure 3.4. Forest plot showing overall pooled hypertension prevalence in Africa in 2000

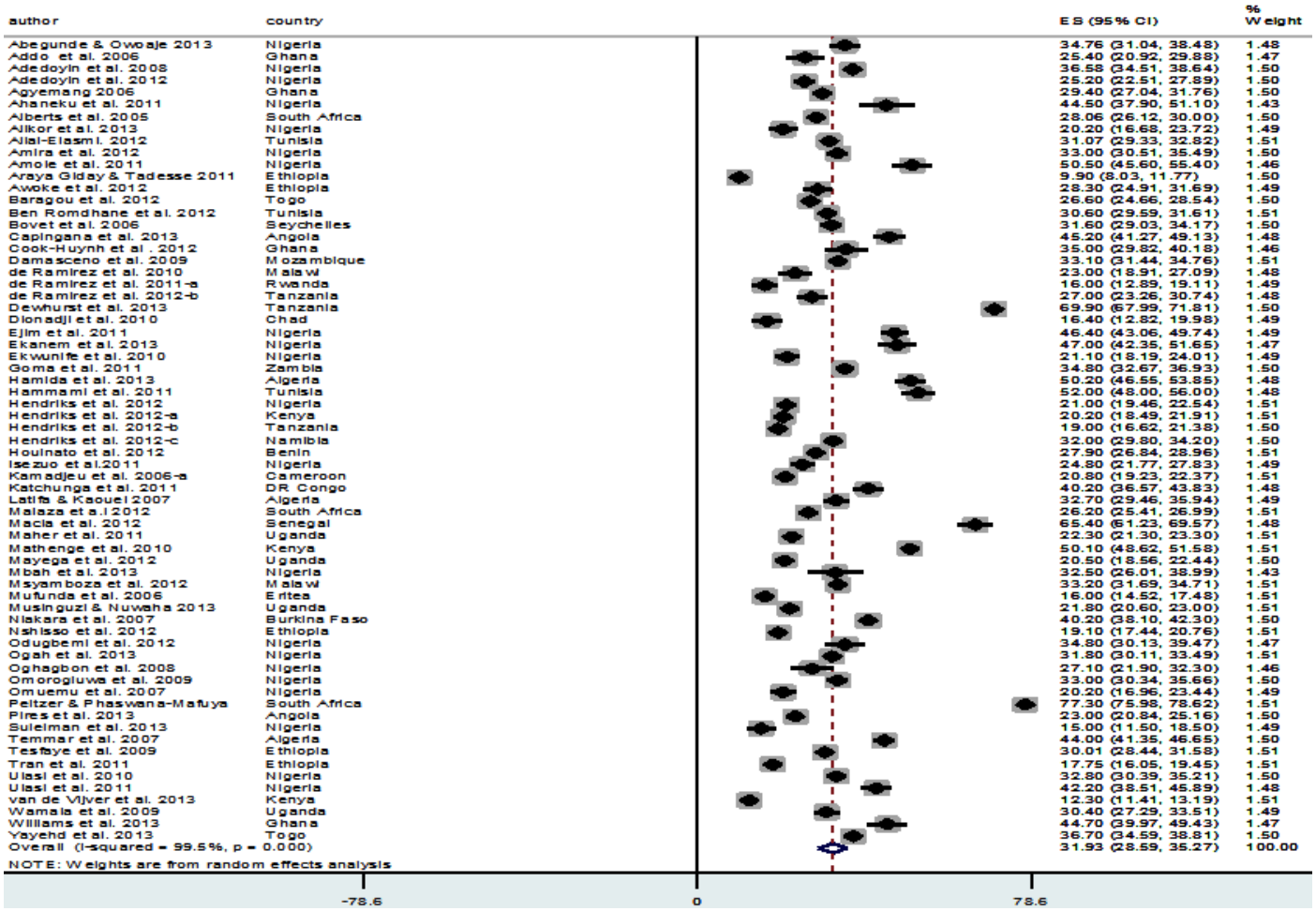

Figure 3.5. Forest plot showing overall pooled hypertension prevalence in Africa in 2010

Table 3.4. Overall pooled hypertension prevalence in Africa

Year	*Setting*	*Overall sample size*	*Mean age*	*Mean Blood Pressure*		*Prevalence of hypertension*			*Awareness rate (% (se))*
				Mean systolic BP (se)	*Mean diastolic BP (se)*	*Both sexes (se)*	*Male (se)*	*Female (se)*	
1990	Mixed	21416	44.1	123.8 (2.2)	77.5 (1.1)	20.5 (2.9)	23.0 (3.3)	20.2 (3.5)	16.9 (3.9)
	Urban	6925	39.4			17.2 (3.5)	21.1 (4.0)	15.1 (3.5)	
	Rural	5796	48.8			11.1 (2.1)	9.4 (3.0)	8.3 (4.4)	
2000	Mixed	38294	51.2	126.9 (1.8)	77.2 (0.9)	31.0 (2.1)	26.9 (2.1)	28.4 (2.5)	29.2 (4.5)
	Urban	20898	45.7			26.1 (1.9)	26.8 (1.5)	23.9 (1.9)	
	Rural	11377	55.2			26.3 (2.3)	24.5 (3.2)	25.7 (3.1)	
2010	Mixed	126754	47.1	126.9 (1.1)	79.4 (0.5)	31.9 (1.6)	29.7 (1.9)	31.4 (2.1)	33.7 (3.9)
	Urban	44114	47.4			29.6 (2.1)	28.2 (2.3)	28.4 (2.5)	
	Rural	46669	48.6			29.0 (2.3)	26.9 (2.7)	30.1 (2.9)	

se: standard error

Table 3.5. Regional pooled hypertension prevalence in Africa

African regions	*Overall sample size*	*Mean age*	**Mean Blood Pressure**		**Prevalence of hypertension**			**Awareness rate (% (se))**
			Mean systolic BP (se)	**Mean diastolic BP (se)**	**Both sexes (se)**	**Male (se)**	**Female (se)**	
North	28046	54.3	129.6 (1.6)	78.0 (0.8)	33.3 (2.6)	29.6 (2.1)	35.5 (2.6)	36.2 (9.2)
Sub-Saharan Africa	169429	46.4	125.6 (0.9)	78.9 (0.5)	27.8 (1.4)	27.8 (1.6)	27.8 (1.7)	30.6 (3.1)
Central	24206	43.7	119.2 (1.8)	75.4 (0.9)	21.1 (2.7)	21.5 (3.1)	19.3 (2.9)	25.1 (4.2)
East	53312	46.0	127.5 (2.2)	79.3 (0.8)	26.8 (2.9)	25.0 (2.8)	26.1 (3.4)	40.9 (6.9)
South	34753	47.5	123.5 (2.3)	79.4 (0.9)	34.6 (4.2)	35.4 (5.1)	34.2 (4.6)	26.4 (7.0)
West	57417	46.9	128.2 (0.9)	79.8 (0.8)	27.3 (1.5)	29.6 (1.8)	28.2 (1.9)	21.7 (2.7)

se: standard error

Modelled estimates of hypertension prevalence and cases in Africa

The epidemiological modelling indicated the overall cases and prevalence of hypertension in Africa has been increasing since 1990 (See **Appendix 2** for summary of data used in modelling). In adults aged ≥20 years, 54.6 million cases of hypertension were estimated in 1990 with an age-adjusted prevalence of 19.1% (13.9, 25.5), 92.3 million cases in 2000 with an age-adjusted prevalence of 24.3% (23.3, 31.6), and 130.2 million cases in 2010 with an age-adjusted prevalence of 25.9% (23.5, 34.0). The general sex distribution revealed the prevalence of hypertension were higher among men than women. Among men, about 29.8 million cases of hypertension were estimated in 1990 (21.2%, 95%CI: 16.5-29.6), 46.8 million cases in 2000 (25.1%, 95%CI: 22.9-31.0), 64.8 million cases in 2010 (26.1%, 95%CI: 23.6-33.6). However, among women, about 24.8 million cases of hypertension were estimated in 1990 (17.1%, 95%CI: 13.4-27.0), 45.5 million cases in 2000 (23.6%, 95%CI: 21.5-33.3), 65.4 million cases in 2010 (25.7%, 95%CI: 21.7-35.4) (see **Tables 3.6-3.8,** and **Figures 3.6-3.8)**

Table 3.6. Estimated hypertension prevalence rates and cases in Africa in both sexes (estimates derived from epidemiological model and the UN population demographics)

Age (years)	*1990*		*2000*		*2010*	
	Prevalence (%) = $8.7962e^{0.0161x}$	Hypertension cases (000)	Prevalence (%) = $11.822e^{0.0177x}$	Hypertension cases (000)	Prevalence (%) = $9.796e^{0.0235x}$	Hypertension cases (000)
20-24	12.5	6961.279	17.5	13134.411	16.4	15969.503
25-29	13.6	6319.733	19.1	11761.160	18.5	15499.070
30-34	14.7	5722.049	20.8	10540.253	20.8	14395.931
35-39	15.9	5125.030	22.8	9662.284	23.4	12993.072
40-44	17.3	5293.178	24.9	8844.815	26.3	11868.440
45-49	18.7	4770.732	27.2	7956.942	29.6	11178.983
50-54	20.3	4416.345	29.7	7076.878	33.2	10531.041
55-59	22.0	4015.862	32.4	6135.655	37.4	9602.545
60-64	23.9	3546.226	35.4	5372.853	42.1	8458.233
65-69	25.9	2935.649	38.7	4436.133	47.3	6989.765
70-74	28.0	2333.696	42.3	3326.293	53.2	5546.874
75-80	30.4	1713.440	46.2	2078.889	59.8	3809.200
80+	35.7	1462.513	55.1	1997.851	75.7	3327.737
Total 20+ (95% CI)	19.1 (13.9-25.5)	54615.730	24.3 (23.3-31.6)	92324.390	25.9 (23.5-34.0)	130170.401

x=mid-point of UN population 5-year age group

Table 3.7. Estimated hypertension prevalence rates and cases in Africa among men (estimates derived from epidemiological model and the UN population demographics)

Age	*1990*		*2000*		*2010*	
	Prevalence (%) = $10.505e^{0.0175x}$	Hypertension cases (000)	Prevalence (%) = $17.771e^{0.0088x}$	Hypertension cases (000)	Prevalence (%) = $10.334e^{0.0223x}$	Hypertension cases (000)
20-24	15.4	4287.483	21.6	8141.867	16.9	8241.670
25-29	16.9	3901.526	22.5	6946.029	18.9	7934.829
30-34	18.4	3542.458	23.6	5932.465	21.1	7345.081
35-39	20.1	3187.968	24.6	5185.153	23.6	6596.039
40-44	21.9	2865.689	25.7	4513.438	26.4	5943.763
45-49	23.9	2535.072	26.8	3859.029	29.5	5490.843
50-54	26.1	2303.794	28.1	3261.431	32.9	5063.796
55-59	28.5	2061.997	29.3	2667.812	36.8	4529.248
60-64	31.1	1755.050	30.7	2197.312	41.2	3918.656
65-69	33.9	1365.244	32.0	1718.733	46.0	3154.577
70-74	37.0	978.408	33.5	1201.287	51.5	2424.530
75-80	40.4	589.023	34.9	695.730	57.5	2238.964
80+	48.2	411.868	38.2	464.571	71.9	1917.733
Total 20+ (95% CI)	21.2 (16.5 -29.6)	29785.580	25.1 (22.9-31.0)	46784.860	26.1 (23.6-33.6)	64799.730

Table 3.8. Estimated hypertension prevalence rates and cases in Africa among women (estimates derived from epidemiological model and the UN population demographics)

Age (years)	*1990*		*2000*		*2010*	
	Prevalence (%) = $7.631e^{0.0195x}$	Hypertension cases (000)	Prevalence (%) = $14.879e^{0.0115x}$	Hypertension cases (000)	Prevalence (%) = $7.6974e^{0.0279x}$	Hypertension cases (000)
20-24	11.7	3253.603	19.2	7188.909	14.2	6879.980
25-29	12.9	3018.326	20.3	6265.350	16.3	6839.885
30-34	14.2	2791.264	21.5	5463.243	18.8	6477.360
35-39	15.7	2548.505	22.8	4870.534	21.6	5970.342
40-44	17.3	2320.801	24.1	4347.172	24.8	5617.575
45-49	19.1	2108.716	25.5	3814.806	28.7	5480.796
50-54	21.1	1978.743	27.1	3309.921	32.8	5355.558
55-59	23.2	1800.967	28.7	2818.021	37.8	5053.976
60-64	25.6	1593.129	30.4	2429.126	43.4	4600.255
65-69	28.2	1289.237	32.2	1960.988	49.9	3955.928
70-74	31.1	976.8551	34.1	1457.391	57.4	3280.345
75-80	34.3	630.250	36.1	906.116	65.9	2970.846
80+	41.6	519.756	40.5	707.961	87.2	2887.797
Total 20+ (95% CI)	17.1 (13.4-27.0)	24830.150	23.6 (21.5-33.3)	45539.541	25.7 (21.7-35.4)	65370.642

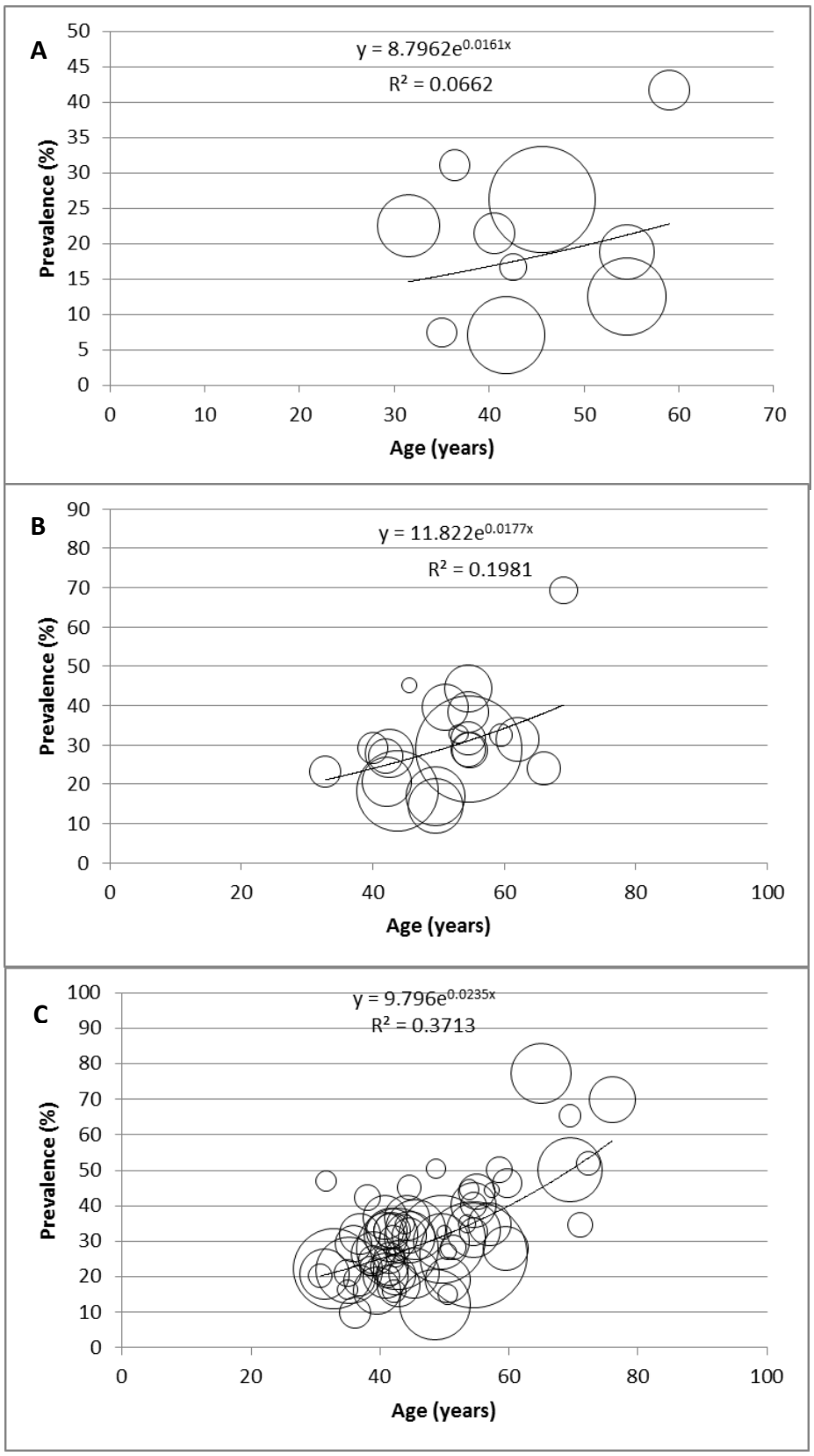

Figure 3.6. Epidemiological model showing relationship between age and crude prevalence of hypertension in both sexes in Africa, with size of bubble corresponding to sample size (A: 1990, B: 2000, C: 2010).

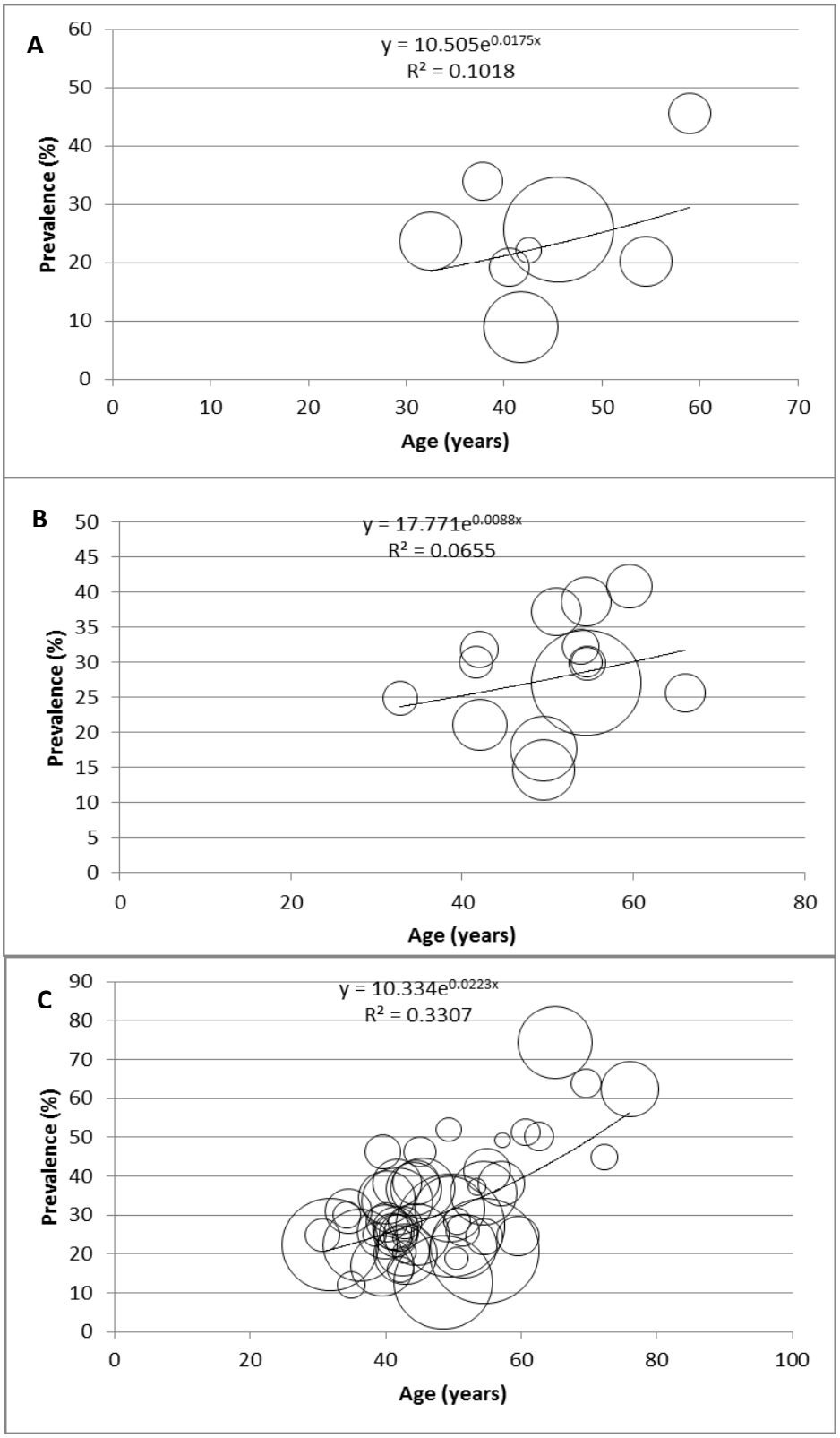

Figure 3.7. Epidemiological model showing relationship between age and crude prevalence of hypertension among men in Africa, with size of bubble corresponding to sample size (A: 1990, B: 2000, C: 2010).

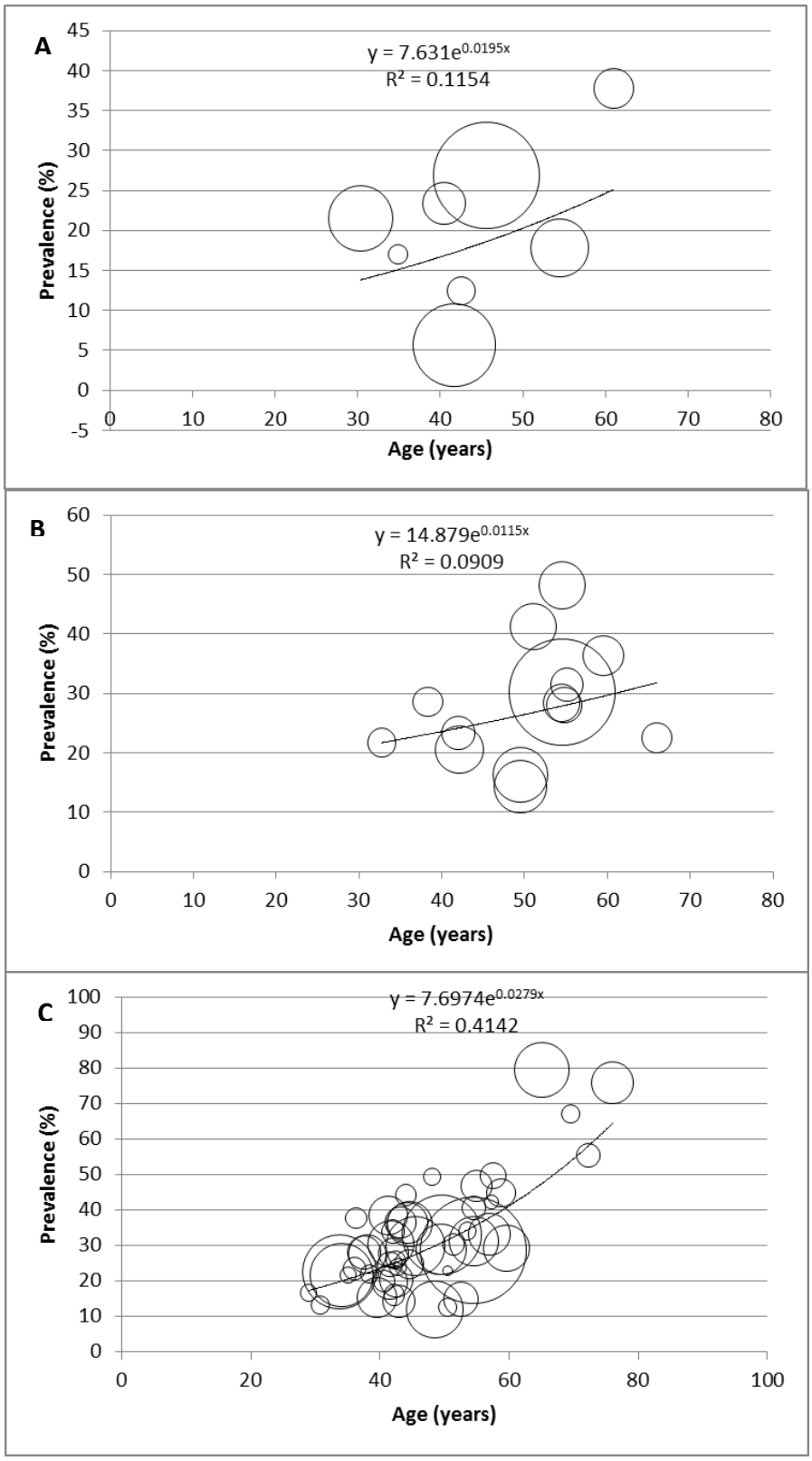

Figure 3.8. Epidemiological model showing relationship between age and crude prevalence of hypertension among women in Africa, with size of bubble corresponding to sample size (A: 1990, B: 2000, C: 2010).

3.2.2 Stroke

Systematic review

The literature search returned 1227 publications from Medline (286), EMBASE (731) and Global Health (210). A further 5 studies were included from other sources (Google Scholar and reference lists of relevant publications). 927 studies remained after removing duplicates. On screening titles for relevance (stroke studies conducted primarily on African populations), 839 studies were excluded, giving a total of 88 full texts that were assessed. After applying the quality criteria, 69 studies were further excluded (32 articles did not provide numerical estimates on incidence and/or prevalence of stroke, and 37 articles did not clarify study designs and survey methodologies). A total of 19 studies were finally retained for the review; all the 19 for qualitative synthesis and 18 for quantitative analysis (**Figure 3.9**).

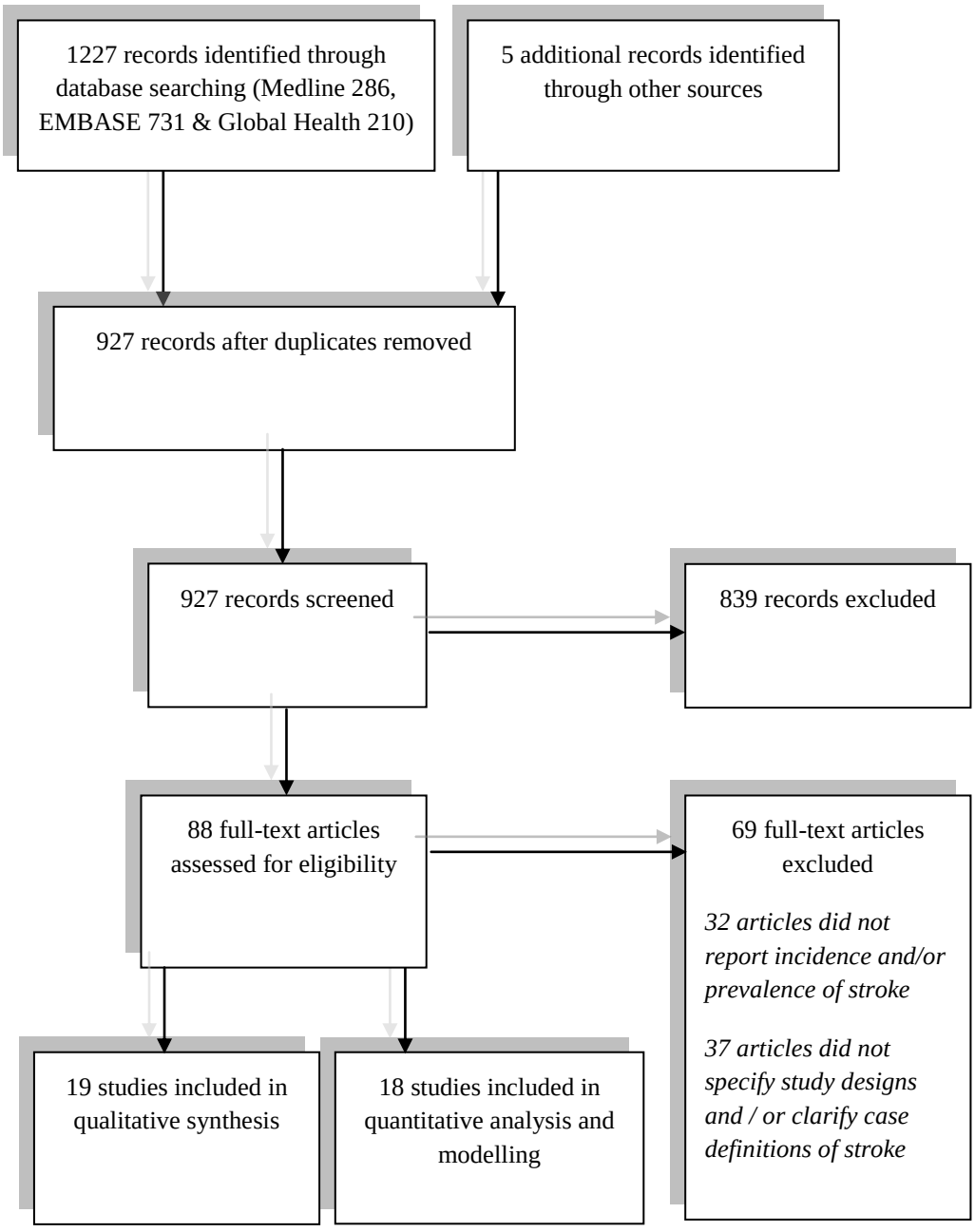

Figure 3.9. Flow diagram of search results for stroke studies in Africa

Study characteristics

The retained 19 studies were conducted across the main regions of Africa (east, north, west and south), but with Northern Africa having the highest output (7 studies). 10 African countries were represented; Egypt and Nigeria ranked highest with 4 studies each, Libya, South Africa and Tanzania had two studies each, while Benin, Ethiopia, Mozambique, Tunisia and Zimbabwe had one study each (**Table 3.9** and **Figure 3.10**). About 57.9% of retained studies (11 studies) were conducted in predominantly urban settings and completed within one year period, respectively. Most studies (18 studies) had a sample size >3000; the total sample size from all retained studies was over 6.3 million, with a mean and median sample size of 332,277 and 60,820 respectively. 14 studies were population-based, of which 8 were community-based door-to-door surveys and 2 studies each were based on demographic health surveys, population/ community-based stroke registries and cross-sectional population-based surveys. There were 5 hospital-based studies with only one from a hospital-based stroke registry. Studies comply with the WHO case ascertainment or a modified definition, while some studies employed cranial computed tomography (CT) or magnetic resonance imaging (MRI) to confirm diagnosis (**Tables 3.9** and **3.10**). Most studies were conducted on the entire study population with an overall mean age of 55.9 years. Across retained studies, age determination of subjects were determined from documented age-verification records, and in the absence of such, historical landmarks were employed.

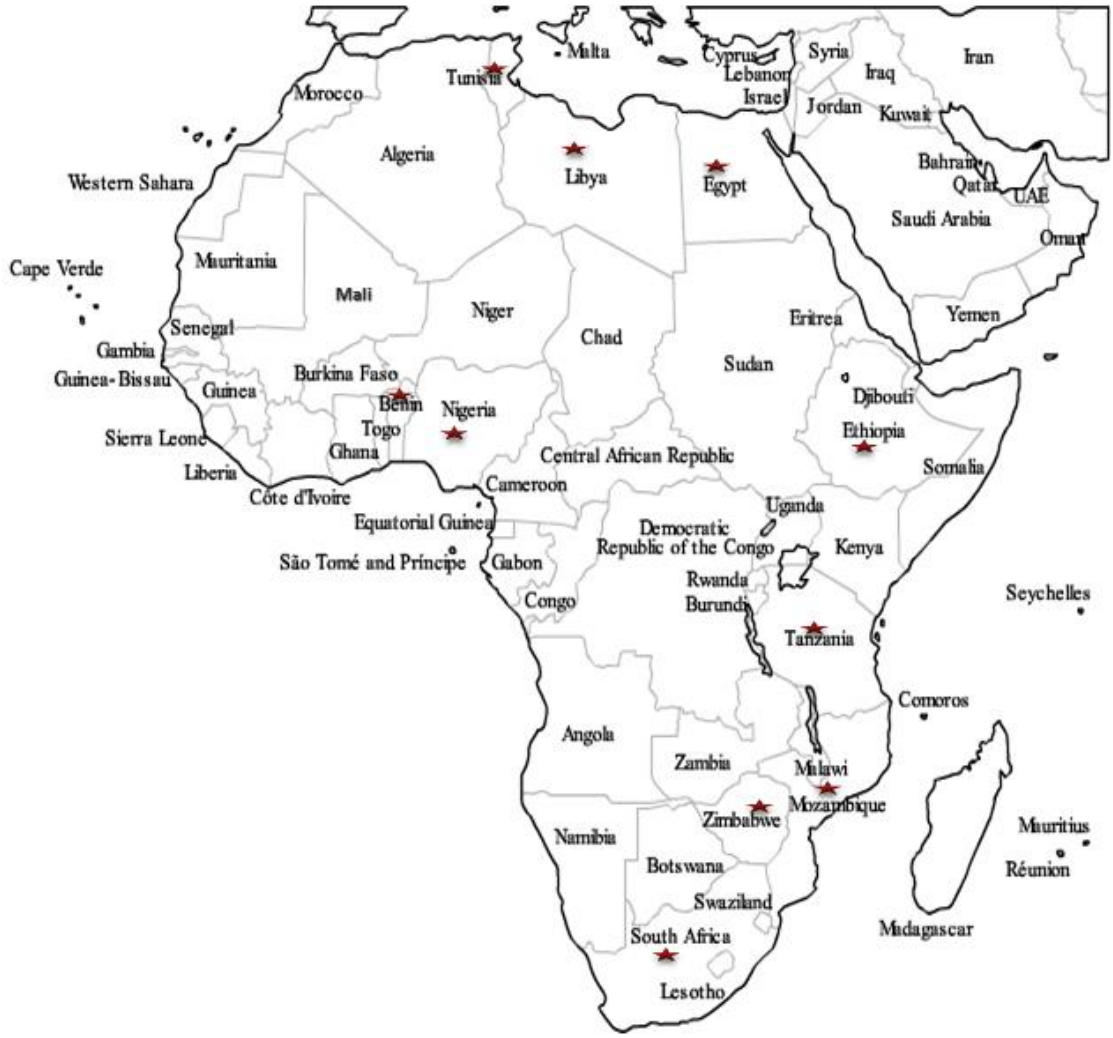

Figure 3.10. Map of Africa with asterisks showing countries of the retained stroke studies

Table 3.9. Characteristic distribution of retained stroke studies in Africa

Characteristics	***Country***	***Study sites***
East (3 studies)	Ethiopia	1
	Tanzania	2
North (7 studies)	Egypt	4
	Libya	2
	Tunisia	1
South (4 studies)	Mozambique	1
	South Africa	2
	Zimbabwe	1
West (5 studies)	Benin	1
	Nigeria	4
Duration of study		
<1 year		11
1-3 years		5
>3 years		3
Sample size		
<1000		-
1001-3000		1
>3000		18
Study setting		
Rural		4
Urban		11
Mixed		4
Study methods		
Hospital-based		5
Population-based		14

Table 3.10. Overall characteristics of retained stroke studies

African region	*Country, Setting*	*Author, Year*	*Study period*	*Survey method*	*Case definition*
East	1) Ethiopia, Rural communities (Tekle-Haimanot et al., 1990)	Tekle-Haimanot et al. 1990	1986-88	A door-to-door survey	WHO definition
	2) Tanzania, Hai District, Rural (Dewhurst et al., 2013a)	Dewhurst et al. 2013	1 November 2009 and 31 July 2010	Point prevalence of stroke estimated from a cross-sectional two-phased community epidemiological survey.	WHO International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)
	3) Tanzania, Hai district & Dares Salaam, Mixed Rural and Urban (Walker et al., 2010)	Walker et al. 2010	2003-06	Stroke Incidence measured in two well defined demographic surveillance sites (DSS) over a 3-year period. Patients who had first-ever or recurrent strokes were included. Patients were excluded in suspected cases of infection or a space-occupying lesion	WHO definition
North	4) Egypt, Al Kharga district, Mixed (Farghaly et al., 2013)	Farghaly et al. 2013	June 1, 2005 to May 31, 2009	A door-to-door screening including every door was carried out using a standardized questionnaire	WHO definition
	5) Egypt, Al Quseir. Urban (El Tallawy et al., 2013)	El Tallawy et al. 2013	July 1, 2009 to January 31, 2012	A door-to-door survey of every household in the district	WHO definition
	6) Egypt, Assuit, Urban (Khedr et al., 2013)	Khedr et al. 2013	January 1 2010 - December 31 2010	Community-based study using a three phase door-to-door survey	WHO definition

	7) Egypt, Sohag, Mixed Urban and Rural (Kandil et al., 2006)	Kandil et al. 2006	January 1st 1992 to April 30, 1993	Multistage, systematic random sampling using a door-to-door survey	WHO definition. Diagnosis confirmed by CT scan and other laboratory investigations creatinine
	8) Libya, Benghazi, Urban (El Zunni et al., 1995)	El Zunni et al. 1995	January 1991 to December 1993	Survey conducted on patients referred from the walk-in polyclinics to the four university hospitals and to a rehabilitation center for the handicapped.	Cranial CT scan was performed on all cases within the first week of onset of stroke
	9) Libya, Benghazi, Urban (Ashok et al., 1986)	Ashok et al. 1986	November 1, 1983 and October 31, 1984	Hospital-based survey conducted on referred patients with neurological problems	Cranial CT was performed on cases within the first week of onset of stroke. Survey based on the US National Survey of Stroke guidelines
	10) Tunisia, Kelibia, Mixed Urban and Rural (Attia Romdhane et al., 1993)	Attia Romdhane et al. 1993	1985	Population-based survey	WHO definition and neurologic tool
South	11) Mozambique, Maputo, Urban (Damasceno et al., 2010)	Damasceno et al. 2010	August 1, 2005, to July 31, 2006	Hospital-based survey using the STEPS Stroke questionnaire. Both first-ever and recurrent stroke events were registered	WHO definition: "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin."
	12) South Africa, Agincourt Health and Population Unit, Limpopo province, Rural (Connor, 2004)	Connor et al. 2004	August 2001-October 2002	Point prevalence of stroke survivors measured through door-to-door demographic health survey. Person's first-ever-in-a-lifetime event was recorded	WHO definition: "rapidly developing signs of focal (or global) disturbance of cerebral function, leading to death or lasting longer than 24 hours, with no apparent cause other than vascular". Person's first-ever-in-a-lifetime event was recorded

	13) South Africa, Atteridgeville and Mamelodi suburban areas of Pretoria, Urban (Rosman, 1986)	Rosman 1986	May 1 1984-April 30 1985	Prospective hospital-based survey. Included all strokes (first-ever and recurrent)	Diagnosis confirmed by cranial CT
	14) Zimbabwe, Harare, Urban (Matenga, 1997)	Matenga 1997	Jan- Dec 1991	A hospital-based stroke registry survey. Only first-ever strokes were included	Stroke was defined according to the WHO definition. None had CT
West	15) Benin, Cotonou, Urban (Cossi et al., 2012)	Cossi et al. 2012	September 15, 2008- May 15, 2009	A three-phase door-to-door study was performed	Diagnosis of stroke was confirmed by CT scan evaluation
	16) Nigeria, Ibadan, Urban (Osuntokun et al., 1979)	Osuntokun et al. 1979	1973-75	Population-based stroke registry survey	WHO definition
	17) Nigeria, Igbo-Ora, Rural (Osuntokun et al., 1987)	Osuntokun et al. 1987	1982	Community-based door-to door survey	WHO definition
	18) Nigeria, Lagos, Urban (Danesi et al., 2013)	Danesi et al. 2013	January 1st and December 31st 2007	Prospective community-based stroke registry enrolling hospitalized and non-hospitalized first-ever in a lifetime stroke cases presenting at all health facilities	Stroke was defined using the WHO clinical criteria 'sudden onset of focal neurological deficit lasting longer than 24 h or leading to death with no other cause other than a vascular event'
	19) Nigeria, Lagos, Urban (Danesi et al., 2007)	Danesi et al. 2007	June 1, 2005, and May 30, 2006	Population-based, door-to-door survey using modified WHO questionnaire	Stroke defined as "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin."

CT: computed tomography, ICD: International Classification of Disease, WHO: World Health Organization

Details of quality criteria and grading of retained stroke studies in Africa

Of the retained 19 studies, only one study was graded as low quality (**Table 3.11**). Despite a generally well-explained study design, this study was not included in the meta-analysis due to the relatively small sample size as other studies were mainly based on the general population with mean age ranging between 50 and 60 years

Table 3.11. Quality assessment of retained stroke studies in Africa

Study ID*	***Study design***	***Study analysis***	***Study limitations***	***Generalizability to Africa***	***Grading***
3-9, 11-16, 18, 19	Well explained across all studies	Well explained across all studies	Well-presented across all studies	Study population representative of a larger African population	*High*
1, 10, 17	Well explained across all studies	Not well explained in 1	Not well-presented in 10 and 17	Study population not representative of a larger African population in 1, and 17	*Moderate*
2	Well explained	Not well explained	Not well presented	Study population not fairly representative of a larger African population. Study was basically based on an elderly population >70 years	*Low*

see **Table 3.10 for details of Study ID*

Pooled estimates of reported crude stroke incidence rates in Africa

Across studies reporting crude incidences of stroke, there were 6 population/community-based and 5 hospital-based studies. Population-based incidence rates were generally higher ranging from 25.2/100,000 person years (py) and 26.0/100,000 py in Lagos and Ibadan Nigeria in 2007 and 1979 respectively (Danesi et al., 2013, Osuntokun et al., 1979), to 250/100,000 py in Al-Kharga Egypt in 2007 (Farghaly et al., 2013). The hospital-based studies reported lower incidence rates ranging from 30/100,000 py in Harare Zimbabwe in 1991 (Matenga, 1997), to 148.7/100,000 py in Maputo Mozambique in 2006 (Damasceno et al., 2010) (**Table 3.12**). The pooled incidence from random effect meta-analysis of crude population-based incidence rates was 112.94/100,000 py (95% CI= 90.7-135.17, I^2= 97.5%, p = 0.000) (**Figure 3.11**). The hospital-based meta-analysis was lower with a pooled estimate of 77.39/100,000 py (95% CI= 51.31-103.48, I^2= 99.1%, p = 0.000) (**Figure 3.12**).

Pooled estimates of reported crude stroke prevalence rates in Africa

There were 11 studies (all population/community-based) reporting crude prevalences of stroke survivors with prevalence rates ranging from 15/100,000 population in Ethiopia in 1988 (Tekle-Haimanot et al., 1990), to 963/100,000 population in 2010 (Khedr et al., 2013) (**Table 3.13**). Random effect meta-analysis yielded a pooled prevalence rate of 387.93/100,000 population (95% CI= 284.16- 491.70, I^2= 98.8%, p = 0.000) (**Figure 3.13**). As noted in the quality grading, a Tanzanian study reported a prevalence of 2300/100,000 among people aged 70 years above in Hai district in 2010 (Dewhurst et al., 2013a), this was not included in the meta-analysis due to the relatively small sample size as other studies were mostly based on the general population with mean age ranging between 50 and 60 years (**Table 3.13**)

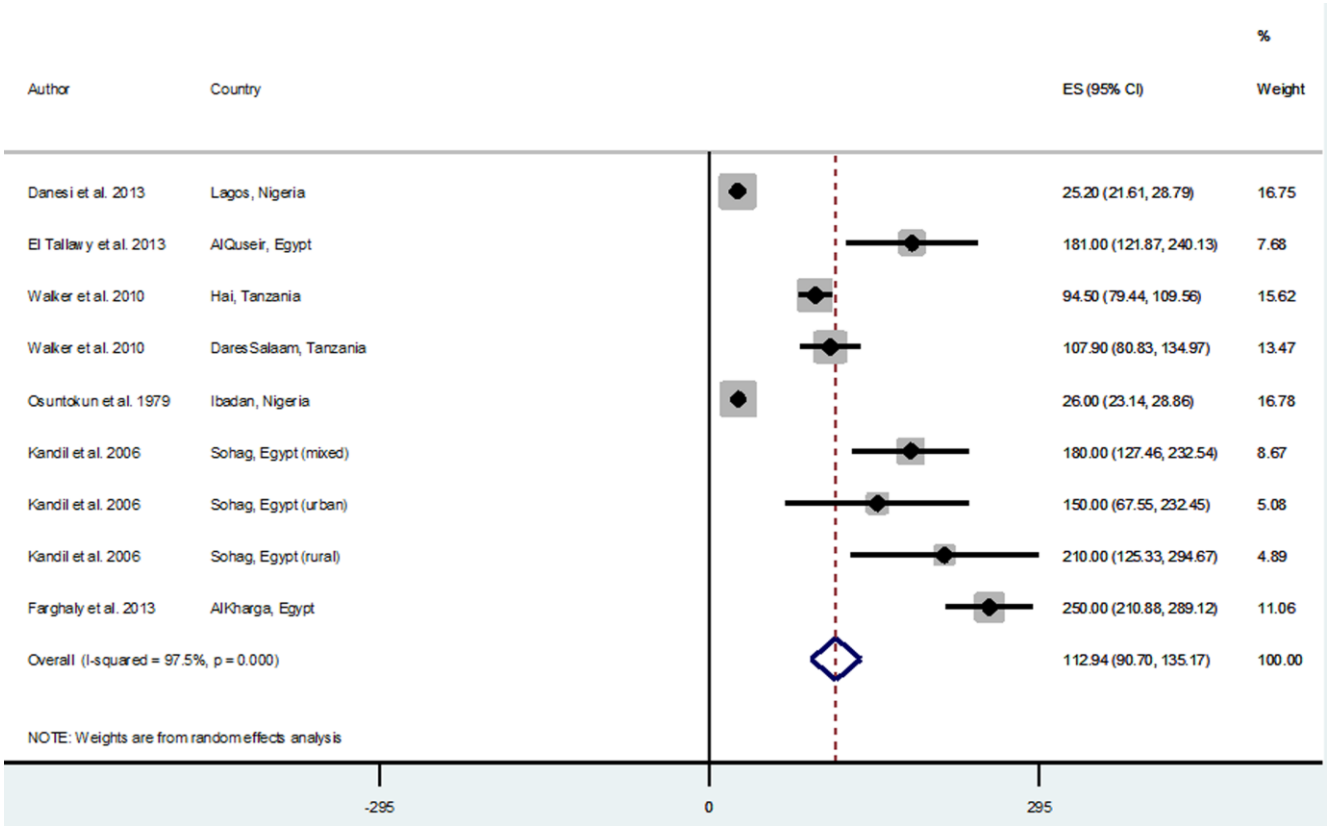

Figure 3.11. Forest plot showing overall pooled incidence of stroke (per 100,000 person years) from population-based studies in Africa.

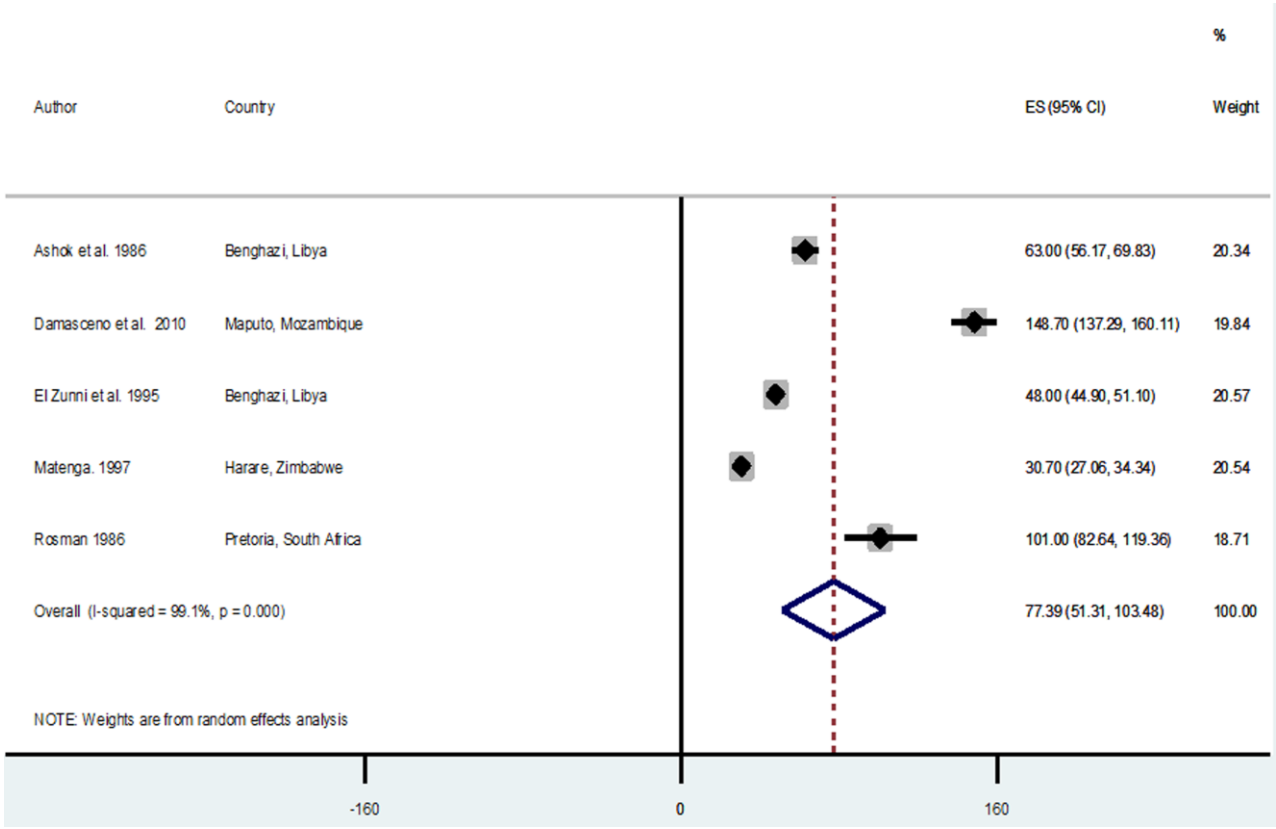

Figure 3.12. Forest plot showing overall pooled incidence of stroke (per 100,000 person years) from hospital-based studies in Africa

Table 3.12. Summary of data from studies reporting crude incidence of stroke in Africa

Author	*Year*	*Age*	*Cases (All)*	*Sample size (All)*	*Incidence /100000 py (All)*	*Cases (Male)*	*Sample size (Male)*	*Incidence /100000 py (Men)*	*Cases (Female)*	*Sample size (Female)*	*Incidence /100000 py (Women)*
POPULATION/COMMUNITY-BASED											
Danesi et al. 2013	2007	All	189	750000	25.2	118	417000	28.3	71	333000	21.3
El Tallawy et al. 2013	2012	20+	36	19848	181	21	9916	212	15	9932	150
Walker et al. 2010a	2006	All	453	159814	94.5	532	71916	106.7	10	87898	76.7
Walker et al. 2010b	2006	All	183	56517	107.9	266	25433	115.2	122	31084	99.7
Osuntokun et al. 1979	1975	All	318	1223077	26	229	538462	25	89	684615	13
Kandil et al. 2006a	1993	All	39	25000	180	21	21000	100	18	21176	85
Kandil et al. 2006b	1993	All	11	8464	150	7	7778	90	4	7547	53
Kandil et al. 2006c	1993	All	20	11228	210	9	9278	97	11	9244	119
Farghaly et al. 2013	2007	All	156	62583	250	86	32165	270	70	30418	230
HOSPITAL-BASED											
Ashok et al. 1986	1984	15+	329	518745	63	184	267590	69	145	251155	58
Damasceno et al. 2010	2006	15+	651	437794	148.7	342	197007	173.6	309	240787	128.3
El Zunni et al. 1995	1993	15+	921	1918750	48	379	1196154	52	322	722596	42
Matenga. 1997	1991	All	273	889250	30.7	142	478114	29.7	131	411136	32
Rosman 1986	1985	20+	116	114931	101	65	60343	108	51	54588	93

Walker et al. 2010a: Hai district (rural setting), Walker et al. 2010b: Dares Salaam district (urban setting)

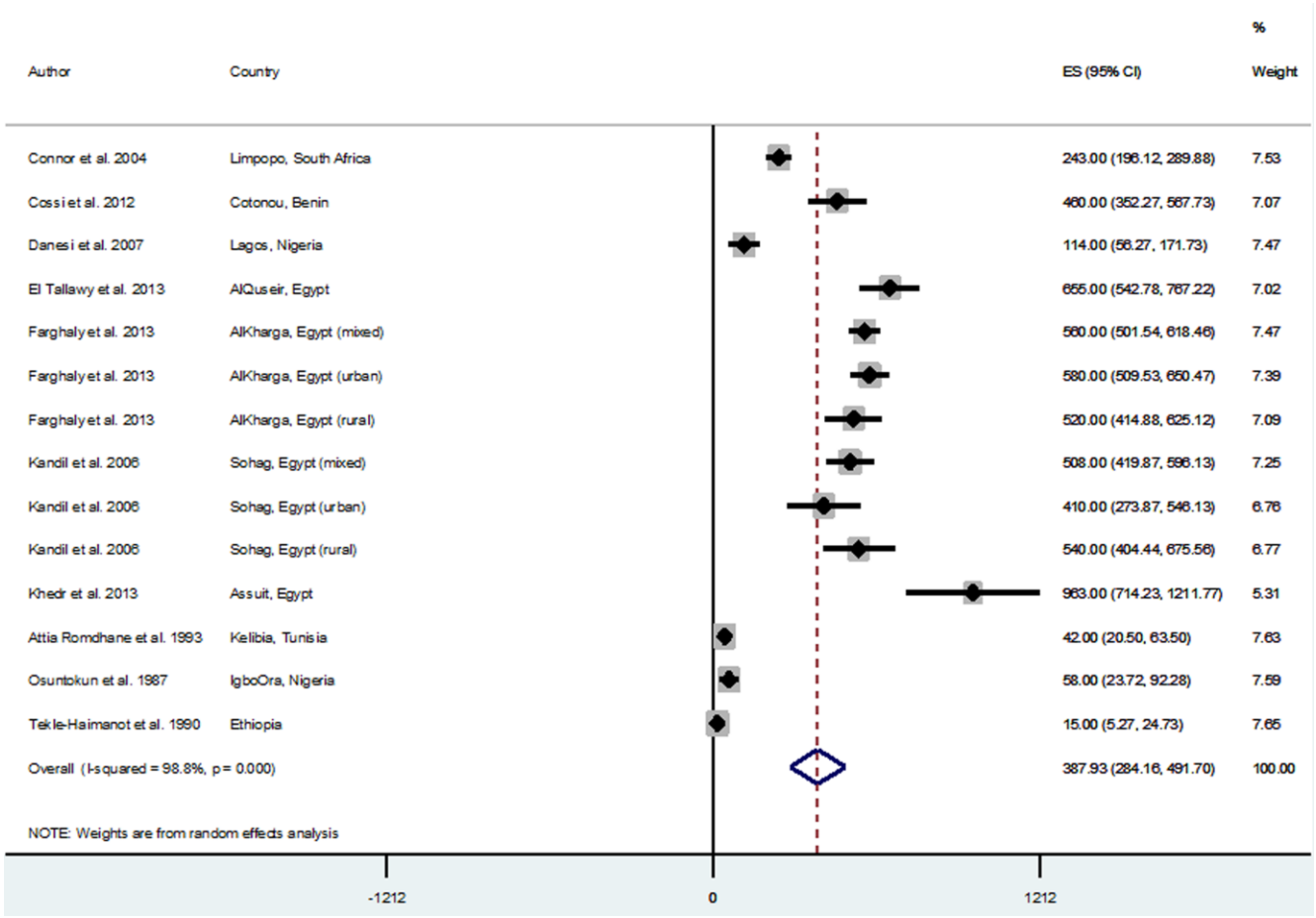

Figure 3.13. Forest plot showing overall pooled prevalence of stroke survivors (per 100,000 population) from population-based studies in Africa.

Table 3.13. Summary of data from studies reporting crude prevalence of stroke survivors in Africa (all population/community-based)

Author, year	*Year*	*Age*	*Cases (All)*	*Sample size (All)*	*Prevalence /100000 (All)*	*Cases (Men)*	*Sample size (Men)*	*Prevalence /100000 (Men)*	*Cases (Women)*	*Sample size (Female)*	*Prevalence /100000 (Men)*
Connor et al, 2004	2002	15+	103	42378	243	37	20042	185	66	22336	296
Cossi et al. 2012	2009	15+	70	15155	460	38	6293	610	32	8862	360
Danesi et al. 2007	2006	All	15	13127	114	11	7295	151	4	5832	69
Dewhurst et al. 2013*	2010	70+	51	2232	2300	29	976	2971	22	1256	1752
El Tallawy et al. 2013	2012	All	130	19848	655	85	9916	860	48	9932	480
Farghaly et al. 2013a	2009	All	351	62583	560	196	32165	610	155	30418	510
Farghaly et al. 2013b	2009	All	257	44600	580	142	22908	620	115	21692	530
Farghaly et al. 2013c	2009	All	94	17983	520	54	9257	580	40	8726	458

Kandil et al. 2006a	1993	All	127	25000	508	65	12500	520	62	12500	490
Kandil et al. 2006b	1993	All	35	8464	410	20	4348	460	15	4116	470
Kandil et al. 2006c	1993	All	61	11228	540	29	5686	510	32	5542	570
Khedr et al. 2013	2010	All	57	5920	963	36	3066	1174	21	2854	736
Attia Romdhane et al. 1993	1985	All	15	34874	42	-	-	-	-	-	-
Osuntokun et al. 1987	1982	All	11	18954	58	-	-	-	-	-	-
Tekle-Haimanot et al. 1990	1988	20-85	9	60820	15	-	-	-	-	-	-

**not included in meta-analysis, a: mixed setting, b: urban setting, c: rural setting*

Modelled estimates of new stroke cases and incidence rates in Africa

Based on the epidemiological model and UN population demographics, new stroke cases and incident rates were estimated for the year 2010.

There were over 496 thousand new cases of stroke in Africa in 2010 among people aged 15 years or more equivalent to 81.3 (13.2-94.9) /100,000 py, with over 312 thousand and over 183 thousand new cases of stroke equivalent to 103.4 (20.7-109.2) /100,000 py and 59.6 (6.9-84.3) /100,000 py among men and women, respectively (**Table 3.14 and Figure 3.14**). Based on the same incidence rates, comparable figures for the year 2000 would amount to 378 thousand new stroke cases, also suggesting an increase of 24% between 2000 and 2010 that is attributable to growth and ageing of the African population alone.

Table 3.14. Estimated new stroke cases and incidence rates in Africa in 2010 (estimates derived from epidemiological model and the UN population demographics)

Age (years)	***Both sexes***		***Men***		***Women***	
	$y = 1.8928e^{0.0793x}$	Stroke cases (000)	$y = 0.9001e^{0.0889x}$	Stroke cases 000)	$y = 0.7204e^{0.0887x}$	Stroke cases 000)
15-19	7.3	7.880	4.1	6.135	3.3	1.745
20-24	10.8	10.531	6.4	8.078	5.1	2.453
25-29	16.1	13.510	9.9	10.205	7.9	3.305
30-34	23.9	16.587	15.5	12.345	12.3	4.242
35-39	35.6	19.788	24.1	14.489	19.2	5.299
40-44	52.9	23.893	37.7	17.135	29.9	6.758
45-49	78.7	29.747	58.7	20.811	46.6	8.935
50-54	116.9	37.040	91.6	25.207	72.6	11.833
55-69	173.8	44.644	142.9	29.510	113.1	15.134
60-64	258.4	51.978	222.9	33.309	176.2	18.669
65-69	384.2	56.777	347.6	35.019	274.5	21.758
70-74	571.2	59.556	542.2	35.104	427.7	24.452
75-79	849.1	54.060	845.6	30.343	666.4	23.718
80+	1601.3	70.413	1722.0	35.221	1355.0	35.192
Total 15+	81.3 (13.23-94.94)	496.405	103.4 (20.74-109.26)	312.911	59.6 (6.85-84.33)	183.494

y= incidence (per 100,000 person years), x=midpoint of age group

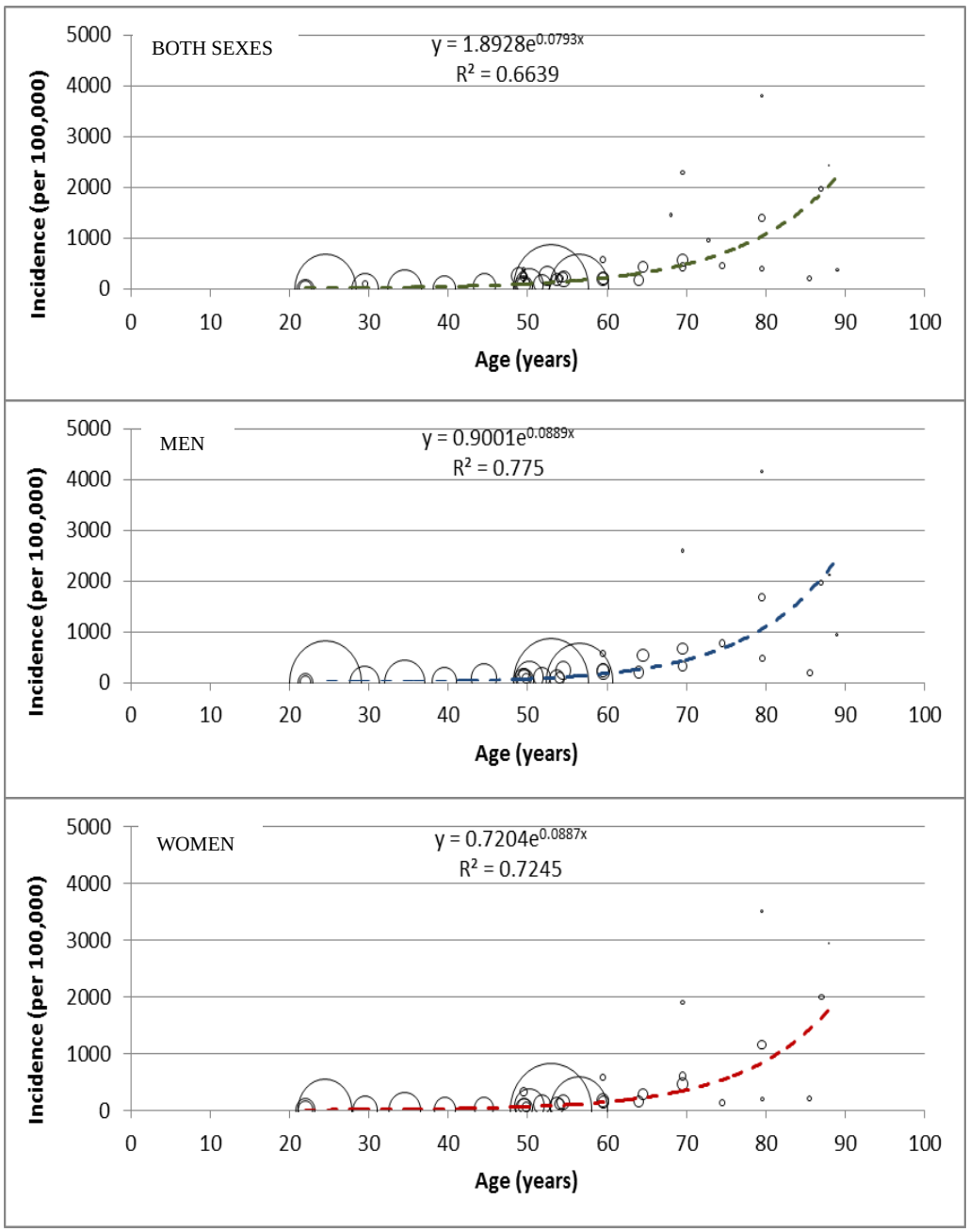

Figure 3.14. Epidemiological model showing relationship between age and crude incidence of stroke in Africa, with size of bubble corresponding to sample size

Modelled estimates of stroke survivors and prevalence rates in Africa

Based on the UN population demographics and bubble graphs derived from all data points, the estimated number of stroke survivors in Africa in 2010 was 1.94 million among people aged 15 years or more with a prevalence of 317.3 (314.0-748.2)/100000 population. There were over 1 million and 922 thousand stroke survivors equivalent to 335.2 (302.3-702.7) /100,000 and 299.7 (268.4-579.0) /100,000 among men and women, respectively (**Table 3.15 and Figure 3.15**). Based on the same prevalence rates, comparable figures for the year 2000 would amount to 1.48 million stroke survivors respectively, also suggesting an increase of 23.7% between 2000 and 2010 that is attributable to growth and ageing of the African population alone.

Table 3.15. Estimated number of stroke survivors and prevalence in Africa in 2010 (estimates derived from epidemiological model and the UN population demographics)

Age (years)	***Both sexes***		***Men***		***Women***	
	$y = 10.045e^{0.0738x}$	Stroke cases (000)	$y = 3.5546e^{0.093x}$	Stroke cases (000)	$y = 1.9743e^{0.0979x}$	Stroke cases (000)
15-19	35.2	15.007	17.3	9.415	10.4	5.592
20-24	50.9	21.660	27.5	13.429	17.0	8.231
25-29	73.7	30.024	43.8	18.411	27.8	11.613
30-34	106.6	39.876	69.7	24.270	45.3	15.606
35-39	154.1	51.449	111.0	31.037	73.9	20.412
40-44	222.9	67.082	176.7	39.827	120.5	27.255
45-49	322.4	90.128	281.2	52.394	196.7	37.735
50-54	466.2	121.133	447.8	68.808	320.9	52.325
55-69	674.3	157.713	712.8	87.642	523.5	70.071
60-64	975.2	198.489	1134.8	107.981	854.1	90.508
65-69	1410.5	234.235	1806.7	123.786	1393.4	110.448
70-74	2039.9	265.449	2876.2	135.482	2273.4	129.967
75-79	2950.3	260.579	4579.0	128.582	3709.0	131.997
80+	5324.5	384.268	9635.8	173.456	8117.0	210.812
Total 15+	317.3 (314.02-748.16)	1937.092	335.2 (302.33-704.71)	1014.520	299.7 (268.36-578.93)	922.572

y=prevalence (per 100,000 population), x=midpoint of age group

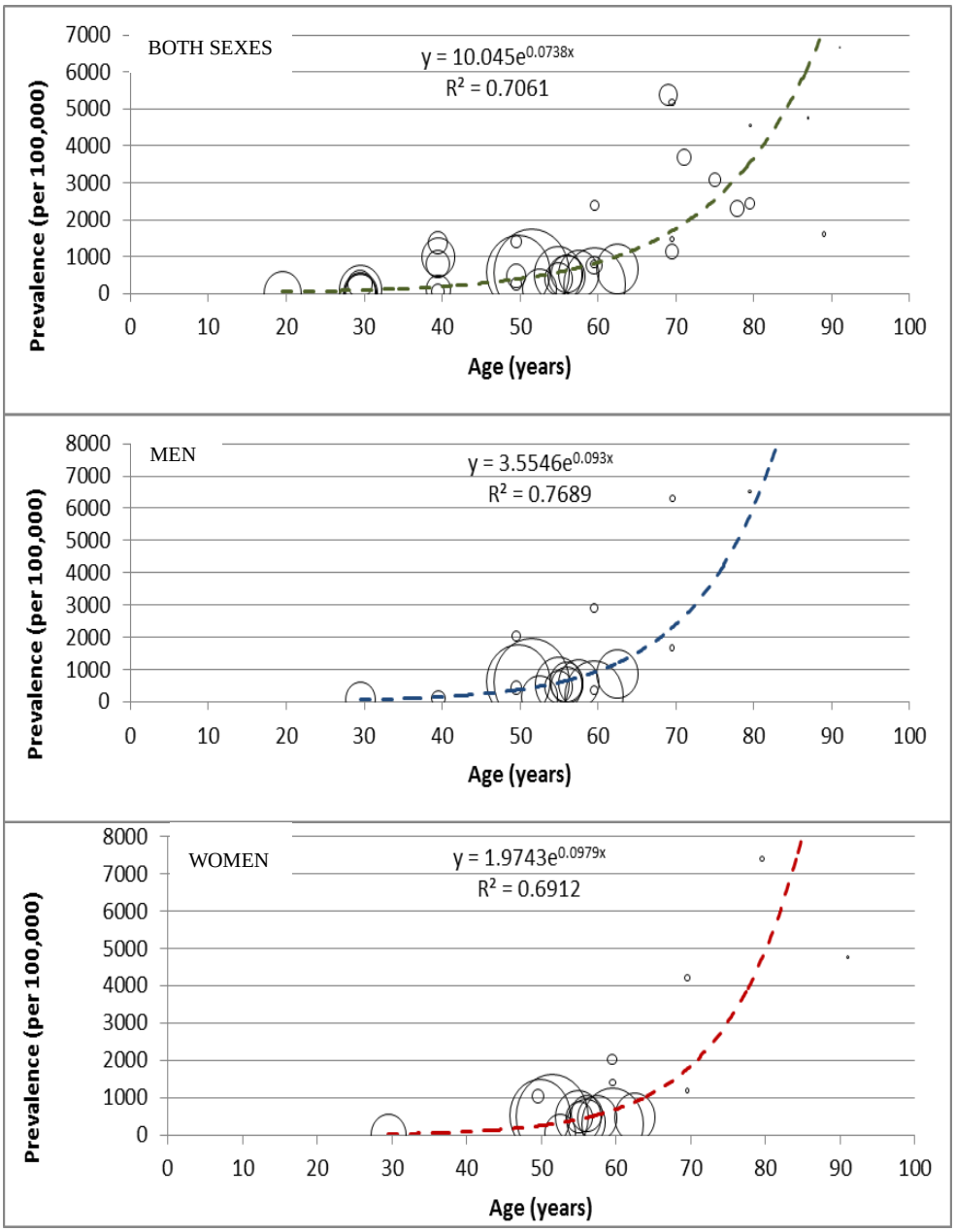

Figure 3.15. Epidemiological model showing relationship between age and crude prevalence of stroke survivors in Africa, with size of bubble corresponding to sample size

3.3 DIABETES

Systematic review

The main literature search returned 3701 publications, with Medline yielding 1183 records, EMBASE 2084, and Global Health 434. Three additional publications were added from other sources including Google Scholar and reference lists of relevant publications identified from an initial scoping review. 2537 records remained after duplicates were excluded. After screening titles for relevance, 2252 studies were excluded, leaving 285 full text articles that were assessed for eligibility. On applying our inclusion, exclusion and quality criteria, 237 studies were excluded (101 articles did not provide prevalence of diabetes or relevant estimates from which prevalence can be calculated , and 136 articles did not specify study designs and / or clarify diabetes case definitions). A total of 48 studies were retained for qualitative and quantitative synthesis (**Figure 3.16**)

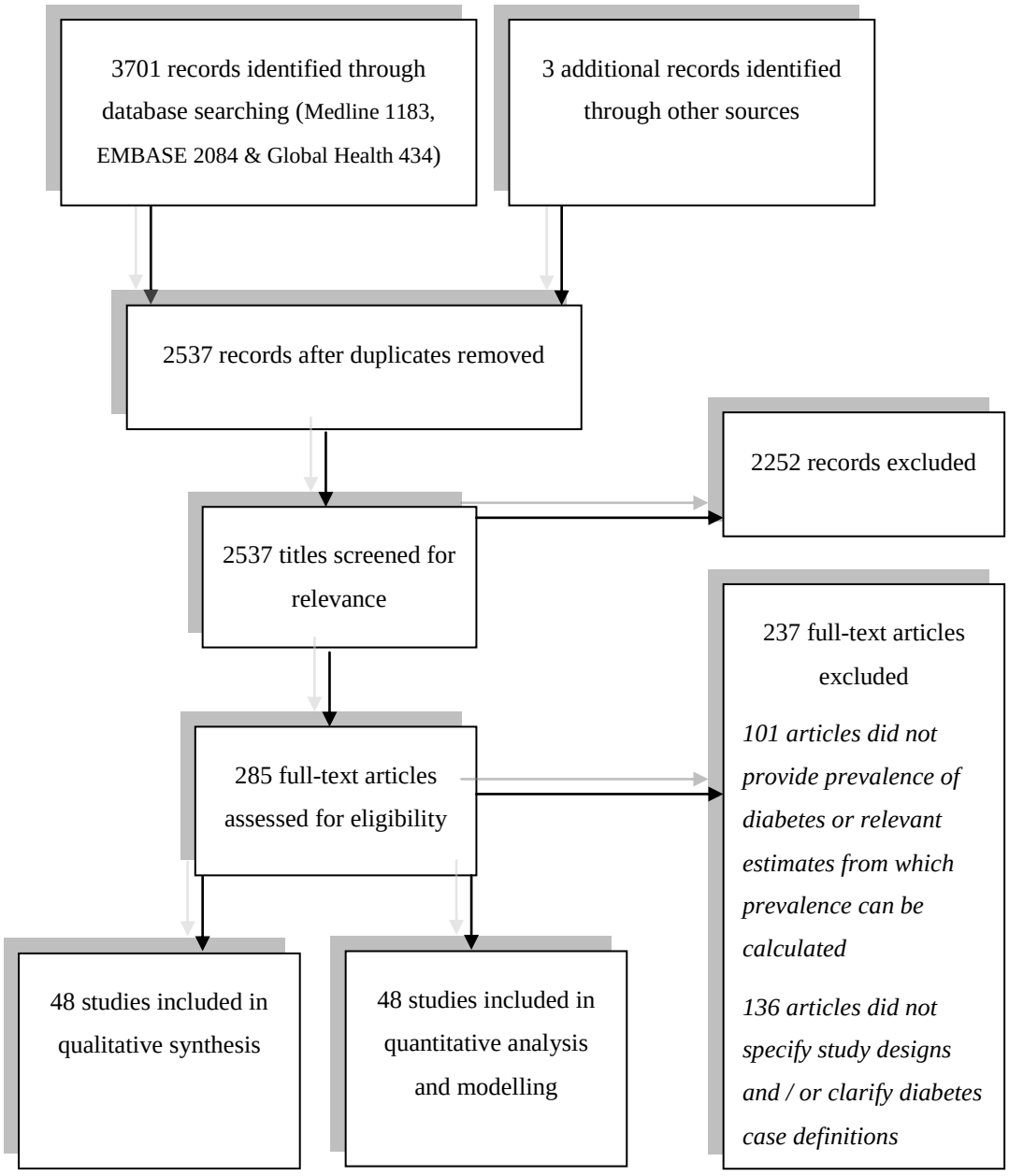

Figure 3.16. Flow diagram of search results of diabetes studies in Africa

Study characteristics

The 48 studies were from 28 African countries, spreading across all parts of Africa. Central Africa had 4 studies, Eastern Africa 9, Northern Africa 7, Southern Africa 12, and Western Africa 16. South Africa and Nigeria had the highest number of studies (7 each), Ghana and Tanzania follows with 3 studies each, while Cameroon, Sudan, Algeria, and Morocco all had 2 studies each (**Table 3.16 and Figure 3.17**).

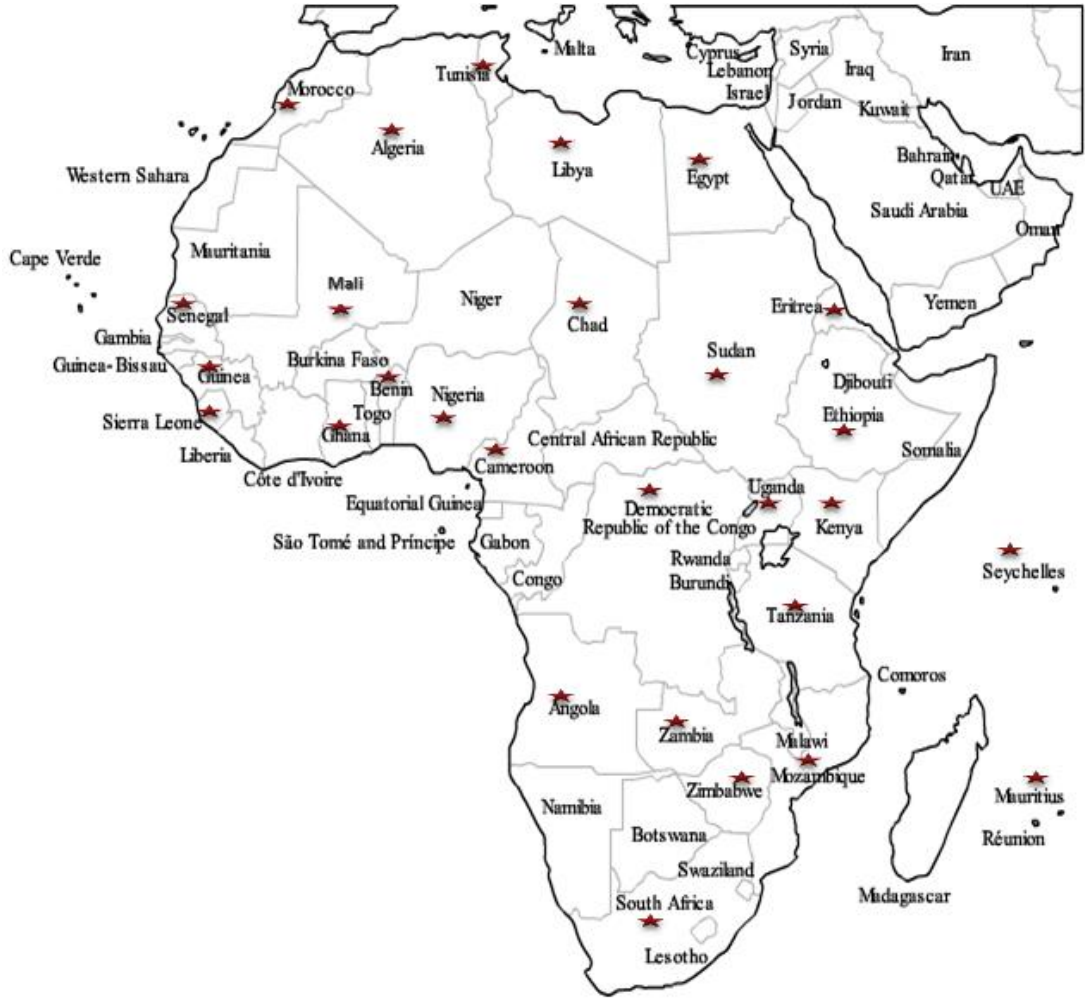

Figure 3.17. Map of Africa with asterisks showing countries of the retained diabetes studies

Table 3.16. Characteristic distribution of retained diabetes studies in Africa

Characteristics	***Country***	***Study sites***
Central (4 studies)	Cameroon	2
	Chad	1
	DR Congo	1
East (9 studies)	Ethiopia	1
	Kenya	1
	Seychelles	1
	Sudan	2
	Tanzania	3
	Uganda	1
North (7 studies)	Algeria	2
	Egypt	1
	Libya	1
	Morocco	2
	Tunisia	1
South (12 studies)	Angola	1
	Mauritius	1
	Mozambique	1
	South Africa	7
	Zambia	1
	Zimbabwe	1
West (16 studies)	Benin	1
	Ghana	3
	Guinea	1
	Mali	1
	Mauritania	1
	Nigeria	7
	Senegal	1
	Sierra Leone	1

Duration of study	
<1 year	21
Years	16
>3 years	11
Sample size	
<1000	24
1001-3000	15
>3000	9
Study setting	
Rural	18
Urban	23
Mixed*	25
Diagnostic criteria (studies overlap)	
WHO 1985	16
WHO 1998	23
WHO-IDF 2006	5
ADA 1997	9
ADA 2003	4

**overlaps with rural and urban sites*

44% of studies were completed within one year, with over 50% carried out in mixed study settings. The total sample size from all retained studies was 102,517. Across individual studies, about 50% of the sample sizes were below 1000, with a mean and median of 1017 and 432 respectively. Many studies applied the WHO 1985 and WHO 1998 diabetes criteria, both representing over 68% of all criteria used. Studies were mostly conducted on people age greater than or equal to 20 years, with an estimated overall mean age of 51.1 years (see **Table 3.17**). For the age determination of subjects across selected studies, birth certificates were mostly employed, and in the absence of valid age-verification documents, subjects' age were determined from historical landmarks.

Table 3.17. Overall characteristics of retained diabetes studies in Africa

African region	*Country, Setting*	*Study period*	*Diagnostic criteria*	*Mean age (years)*	*Prevalence (%)*	*Newly diagnosed (% of diabetes cases)*
Central	1) Cameroon, urban (Echouffo-Tcheugui et al., 2012)	2011	WHO 1998	43.7	14.4	41.2
	2) Cameroon, mixed (Mbanya et al., 1997)	1995	WHO 1985	49	1.02	80
	3) Chad, rural (Dionadji et al., 2010)	2004	WHO 1998	59.4	7.4	-
	4) DRCongo, mixed (On'Kin et al., 2008)	2005	WHO 1998; ADA 1997/2003	46	10	93.5
	5) Ghana (Amoah et al., 2002)	2000-01	WHO 1998 & ADA 1997	44.3	6.4	69.7
East	6) Ethiopia, mixed (Nshisso et al., 2012)	2009-10	WHO-IDF 2006	57	6.5	-
	7) Kenya, mixed (Christensen et al., 2009)	2005	WHO 1998	38.6	4.2	36
	8) Seychelles, mixed (Faeh et al.)	2004-05	ADA 2003	45.2	11.5	46
	9) Sudan, mixed (Elbagir et al., 1996)	1994-95	WHO 1985	59.5	3.4	63.6
	10) Sudan, mixed (Elbagir et al., 1998)	1997	WHO 1985	59.4	8.3	61.4
	11) Tanzania, mixed (Aspray et al., 2000)	1996-97	WHO 1998	54.5	2.8	80
	12) Tanzania, rural (McLarty et al., 1989)	1987	WHO 1985	37	0.87	-
	13) Tanzania, urban (Njelekela et al., 2009)	2007	WHO 1998	59.7	6.0	-
	14) Uganda, rural (Maher et al., 2011b)	2008-09	WHO 1998 & ADA 1997	48	0.4	56.5

North	15) Algeria, mixed (Malek et al., 2001)	2000	WHO 1998 & ADA 1997	47	8.2	50.0
	16) Algeria, mixed (Zaoui et al., 2007)	2006	WHO 1998	59.5	14.2	-
	17) Egypt, mixed (Herman et al., 1995)	1992-94	WHO 1985	59.7	9.3	43.0
	18) Libya, urban (Kadiki and Roaeid, 2001)	2000	WHO 1998 & ADA 1997	57	14.1	64.7
	19) Morocco, mixed (Essiarab et al., 2011)	2010	WHO 1998	54.48	38.6	-
	20) Morocco, mixed (Tazi et al., 2003)	2000	ADA 1997	57	8.4	-
	21) Tunisia, mixed (Gharbi et al., 2002)	2001	WHO 1998	42.5	7.2	33.3
South	22) Angola, rural (Evaristo-Neto et al., 2010)	2008-09	WHO 1998	54.3	2.8	-
	23) Mauritius, mixed (Soderberg et al.)	1987, 1992, 1998	WHO 1985	43.1	12.8	60.9 (1987), 53.0 (1992), 49.1 (1998)
	24) Mozambique, mixed (Silva-Matos et al., 2011)	2005	WHO 1998	44.5	3.5	87.0
	25) South Africa, mixed (Charlton et al., 1997)	1993	WHO 1985	73.8	28.7	25
	26) South Africa, urban (Erasmus et al., 2001)	1992	WHO 1985	57	18.1	18.1
	27) South Africa, urban (Erasmus et al., 2012)	2000	WHO 1998	67	2.45	-
	28) South Africa, rural (Groenewald et al., 2007a)	2007	WHO-IDF 2006	46	7.6	32.8
	29) South Africa, mixed (Levitt et al., 1993)	1990	WHO 1985	56	6.3	-
	30) South Africa, rural (Motala et al., 2008)	2003	WHO 1985/1998; ADA 1997/2003	46.9	4.6	-
	31) South Africa, urban (Peer et al., 2012)	2008-09	WHO 1998	43.3	14.9	36.9

	32) Zambia, urban (Nsakashalo-Senkwe et al., 2011)	2007	ADA 1997 & 2003	59.7	5.1	27.0
	33) Zimbabwe, mixed (Hakim et al., 2005)	2005	WHO 1998	59.7	3.7	34
West	34) Benin, urban (Djrolo et al., 2012)	2011	WHO-IDF 2006	59.4	4.6	75.3
	35) Ghana, rural (Cook-Huynh et al., 2012)	1998	WHO 1998	52	7.7	-
	36) Ghana, mixed (Vuvor et al.)	2009-10	WHO 1998	55	3.85	-
	37) Guinea, mixed (Balde et al., 2007)	2003	WHO 1998 & ADA 1997	49.4	6.1	70.2
	38) Mali, rural (Fisch et al., 1987)	1987	WHO 1985	59.4	0.92	-
	39) Mauritania, mixed (Ducorps et al., 1996)	1984-85	WHO 1985	34.6	1.88	71.4
	40) Nigeria, mixed (Ezenwaka et al., 1997)	1994-95	WHO 1985	60.8	1.6	-
	41) Nigeria, mixed (Nyenwe et al., 2003)	2000	WHO 1998	48.9	6.8	-
	42) Nigeria, urban	2010-11	WHO-IDF 2006	49	4.7	-
	43) Nigeria, rural (Ojewale and Adejumo, 2012)	2002-05	WHO-IDF 2006	42.1	2.5	26.5
	44) Nigeria, urban (Olatunbosun et al., 1998)	1995	WHO 1985	40.8	0.8	71.4
	45) Nigeria, urban (Dahiru et al., 2008)	2007	WHO 1998	59.4	2.0	-
	46) Nigeria, rural (Owoaje et al., 1997)	1995	WHO 1985	62	2.8	-
	47) Senegal, urban (Duboz et al., 2012)	2009	ADA 1997	57	17.8	90.7
	48) Sierra Leone, mixed (Ceesay et al., 1997)	1996	WHO 1985	35.7	1.2	-

Details of quality criteria and grading of retained diabetes studies in Africa

Of the retained 48 studies, only two studies were adjudged low quality (**Table 3.18**). These studies were included in the analysis and modelling due to the well explained general study design, as exclusion does not present any significant change in the pooled prevalence of diabetes.

Table 3.18. Quality assessment of retained diabetes studies in Africa

Study ID*	***Study design***	***Study analysis***	***Study limitations***	***Generalizability to Africa***	***Grading***
1-37, 41-43. 45, 47, 48	Well explained across all studies	Well explained across all studies	Well-presented across all studies	Study population representative of a larger African population	*High*
39, 40, 46	Well explained across all studies	Not well explained in 39	Not well-presented in 40 and 46	Study population not representative of a larger African population in the three studies	*Moderate*
38, 44	Well explained	Not well explained	Not well presented	Study population not fairly representative of a larger African population	*Low*

see **Table 3.17 for details of Study ID*

Distribution of diabetes prevalence rates in Africa across retained studies

In a separate analysis of individual studies, isolated high prevalence rates of diabetes were observed in Northern Africa. Across all studies, Morocco recorded highest prevalence (38.4%) in 2011 (Essiarab et al., 2011). Relatively higher diabetes prevalence were also observed in Algeria (14.2%) in 2006 (Zaoui et al., 2007), and Libya (14.1%) in 2000 (Kadiki and Roaeid, 2001). In sub-Saharan Africa, South Africa reported high diabetes prevalence; 28.7% in 1993 (Charlton et al., 1997), 18.1% in 1992 (Erasmus et al., 2001), and 14.9 in 2009 (Peer et al., 2012). Other high diabetes prevalence estimates (≥14%) were reported in Senegal in 2009 (Duboz et al., 2012), and Cameroon in 2011 (Echouffo-Tcheugui et al., 2012). DR Congo had the highest prevalence of IGT, reporting 26.6% in 2005, while corresponding prevalence of diabetes same year was 10.0% (On'Kin et al., 2008). Seychelles recorded highest prevalence (24.2%) of IFG in 2005, and corresponding prevalence of diabetes same year was 11.5% (Faeh et al.) (See **Table 3.17** for details).

Prevalence distribution of newly diagnosed diabetes mellitus across retained studies

There is high prevalence of undiagnosed diabetes across many studies. The mean and median prevalence rates of newly diagnosed diabetic cases from all studies (expressed as percentage of overall diabetic cases) were 54.9% and 54.75%, ranging from 18.1% in South Africa (Erasmus et al., 2001), to an alarming 93.5% in DR Congo (On'Kin et al., 2008) (see **Table 3.17)**

Pooled prevalence estimates of diabetes in Africa

Across all studies, crude prevalence rates of diabetes were consistently lower in females. A random effect meta-analysis of crude prevalence estimates from all studies yielded a diabetes prevalence of 7.5% (95% CI: 6.3-8.7, I-square=97.9%, p = 0.000), with a male prevalence of 7.8% (3.7-11.8) and female prevalence of 6.9% (2.9-10.9) (**Figure 3.18**). IGT was more common than IFG, and also noted that IGT was higher in women than men and IFG vice versa. The estimated IGT prevalence was 10.2% (95% CI: 7.0, 13.5, I-square=99.7%, p = 0.000) with a male prevalence of 9.9% (7.5-12.3), and a female prevalence of 11.3% (8.4-14.2) (**Figure 3.19)**. The estimated IFG prevalence was 5.7% (95% CI: 4.3-7.1, I-square=97.9%, p = 0.000), with a male prevalence of 7.1% (3.9-10.4), and a female prevalence of 4.3% (2.4-6.2) (**Figure 3.20**). **Table 3.19** shows a detailed representation of the pooled prevalence estimates

Table 3.19. Pooled prevalence estimates of diabetes from retained diabetes studies

Reference	***Mean age (years)***	***Both sexes***		***Male***		***Female***	
		Data points	Pooled prevalence % (95% CI)	Data points	Pooled prevalence % (95% CI)	Data points	Pooled prevalence % (95% CI)
Diabetes	49.3	50	7.5 (6.3-8.7)	40	7.8 (3.7-11.8)	40	6.9 (2.9-10.9)
IGT	49.4	21	10.2 (7.0-13.5)	18	9.9 (7.5-12.3)	18	11.3 (8.4-14.2)
IFG	50.5	18	5.7 (4.3-7.1)	13	7.1 (3.9-10.4)	13	4.3 (2.4-6.2)

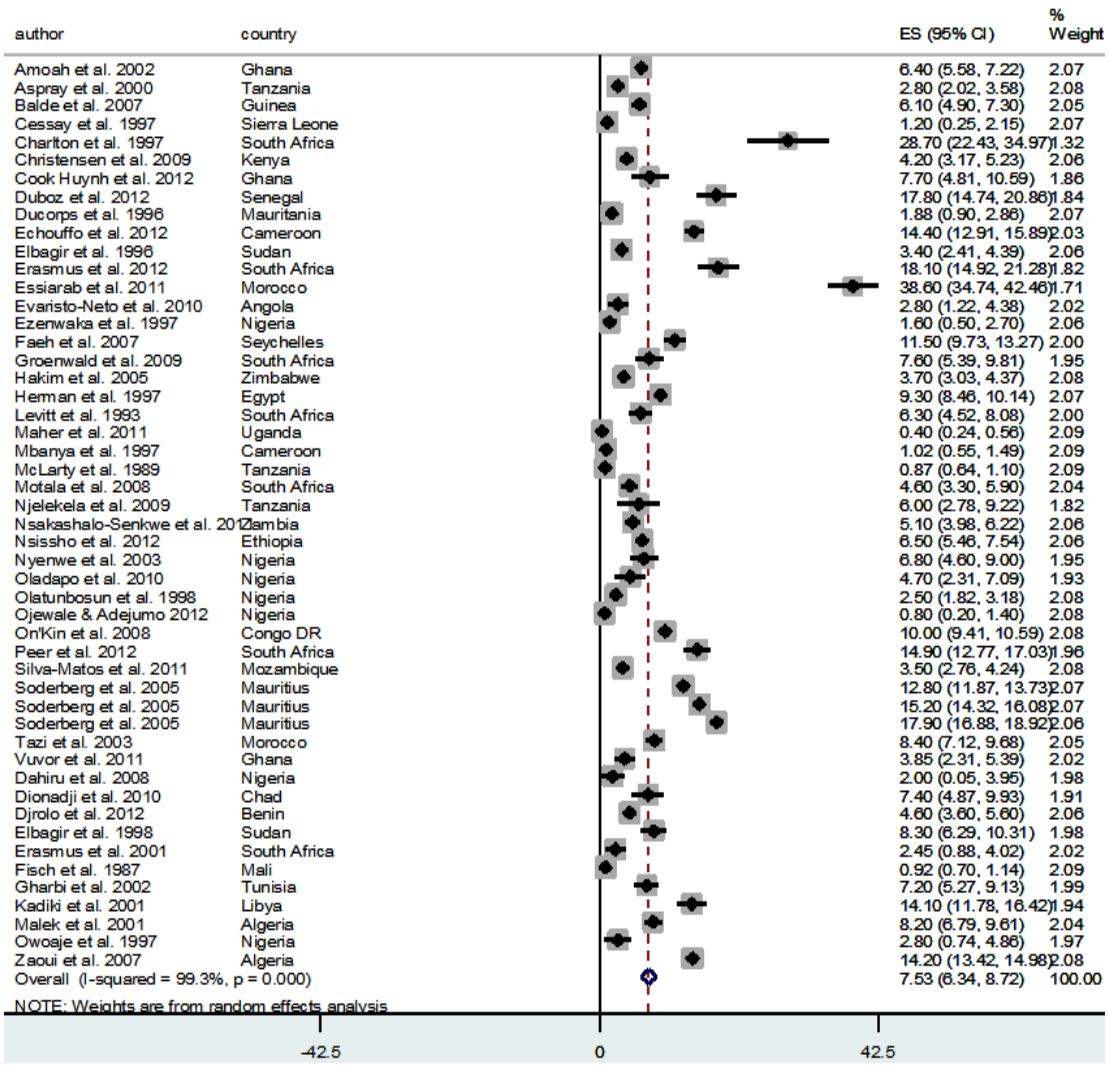

Figure 3.18. Forest plot showing overall pooled prevalence of diabetes in Africa

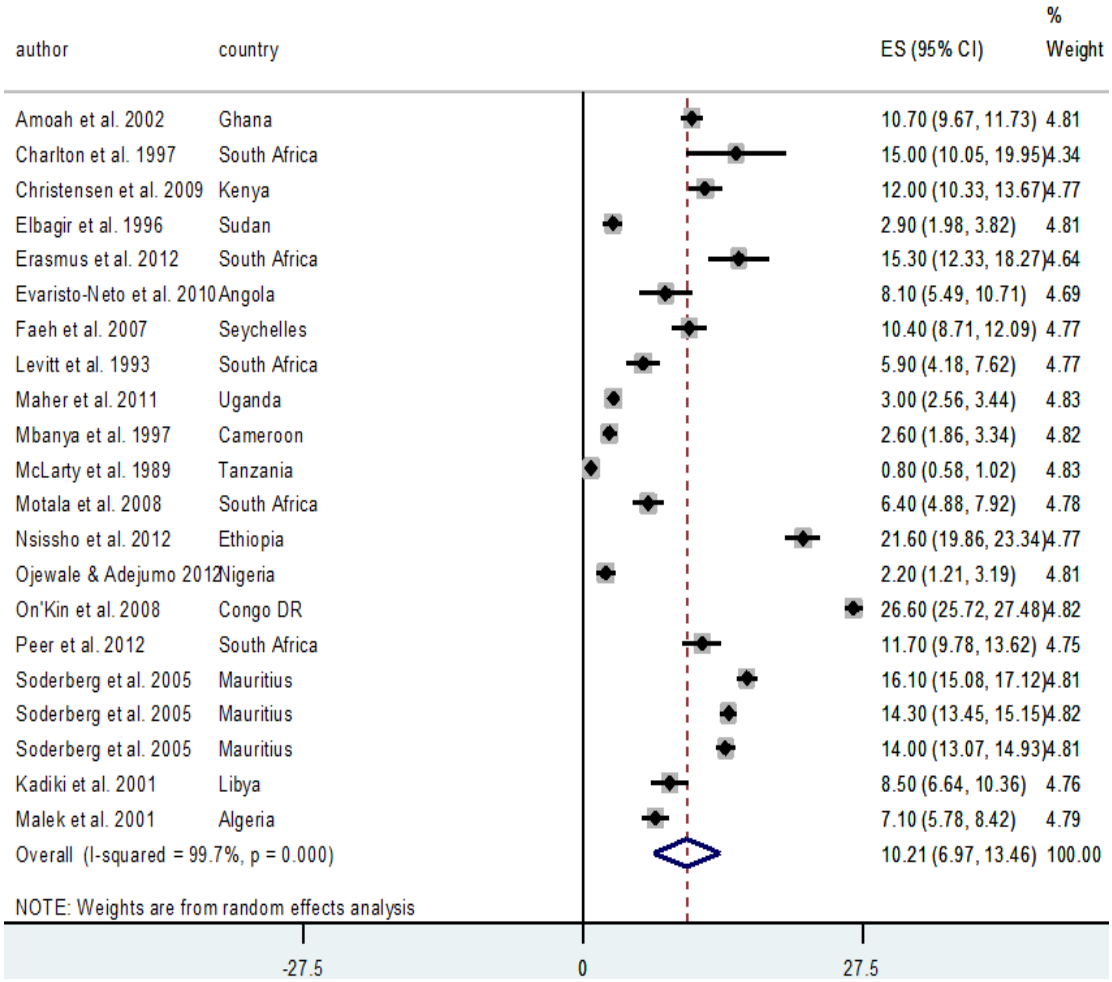

Figure 3.19. Forest plot showing overall pooled prevalence of IGT in Africa

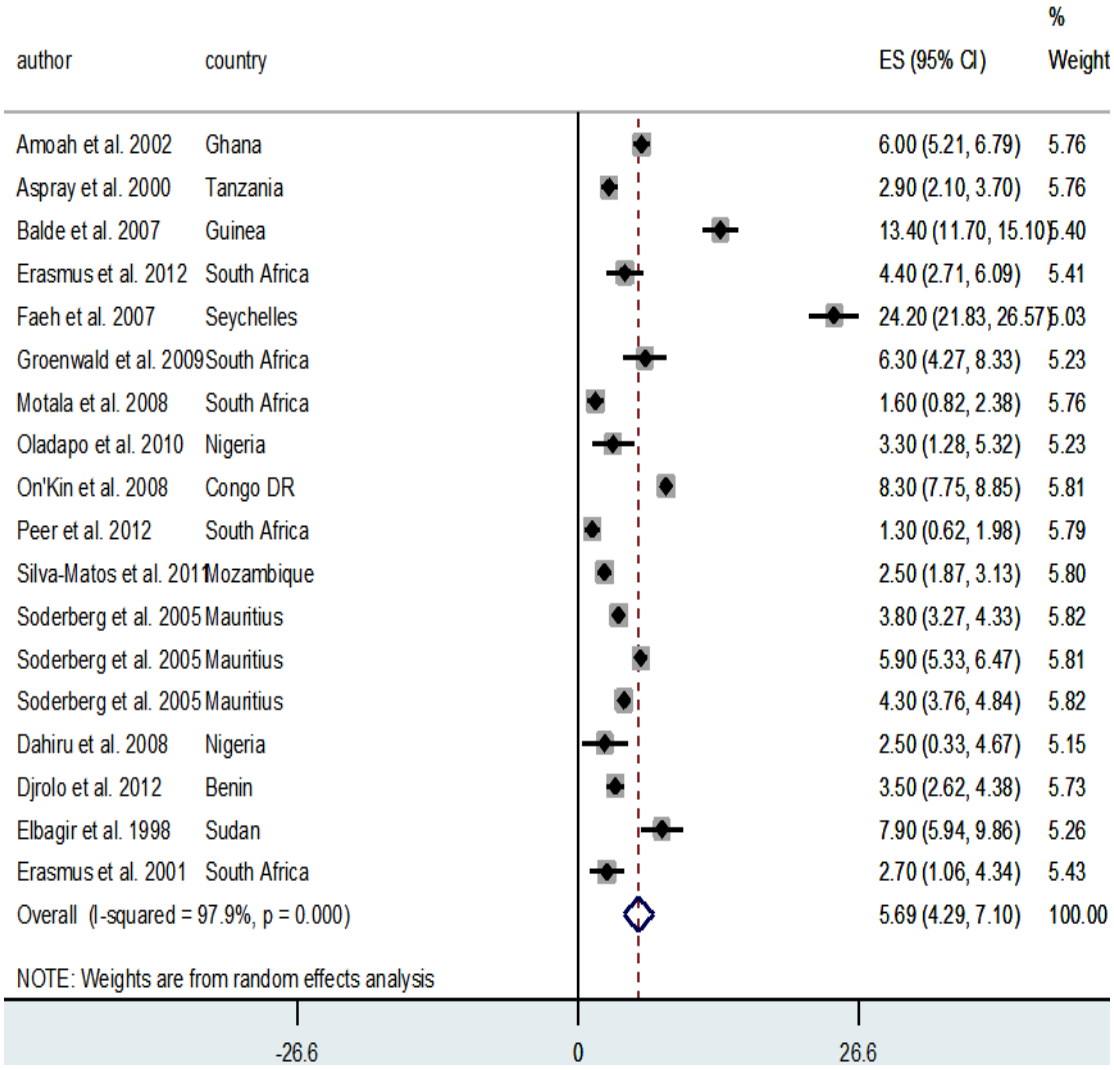

Figure 3.20. Forest plot showing overall pooled prevalence of IFG in Africa

Rural versus Urban diabetes prevalence in Africa

The rural-urban variation was marked for diabetes; we estimated a prevalence of 2.6% (1.3, 4.0) for rural settings, while urban settings had a prevalence of 10.1% (8.0, 12.2) (**Table 3.20**).

For IGT, the rural and urban prevalence were 2.9% (0.9, 4.8) and 7.0% (3.1, 11.0) respectively, while IFG prevalence were 4.6% (3.1, 6.0) and 4.5% (1.4, 7.5) among rural and urban dwellers respectively (**Table 3.20**).

Table 3.20. Rural versus Urban pooled prevalence estimates for Diabetes

	Study setting	***Mean age***	***All***		***Male***		***Female***	
			Data points	Pooled estimate % (95% CI)	Data points	Pooled estimate % (95% CI)	Data points	Pooled estimate % (95% CI)
Diabetes	Rural	48.8	21	2.6 (1.3-4.0)	13	1.3 (0.8-1.8)	13	1.4 (0.5-2.3)
	Urban	51.5	26	10.1 (8.0-12.2)	16	8.2 (5.4-10.9)	16	7.6 (4.5-10.6)
IGT	Rural	47.6	7	2.9 (0.9-4.8)	5	5.3 (3.5-7.0)	5	5.4 (3.0-7.8)
	Urban	49.3	7	7.0 (3.1-11.0)	4	6.0 (1.0-10.9)	4	6.4 (1.7-11.1)
IFG	Rural	47.4	7	4.6 (3.1-6.0)	6	6.1 (4.4-7.8)	6	2.9 (2.2-3.7)
	Urban	53.7	9	4.5 (1.4-7.5)	5	2.8 (1.8-3.7)	5	2.4 (0.8-3.9)

Modelled prevalence estimates

The modelling showed the prevalence of diabetes has been increasing since 1990, with a higher prevalence and diabetes cases observed among women in 2000 and 2010 (See **Appendix 4** for summary of all data used in modelling). In 1990, the prevalence of diabetes was 2.4% (0.9, 4.1), with an estimated 8.5 million diabetes cases among people aged ≥15 years in both sexes, 4.4 million cases among men and 4.1 million cases among women. By 2000, the prevalence slightly increased to 2.9% (1.7, 3.9) accounting for 13.5 million diabetes cases among people aged ≥15 years in both sexes, 6.4 million cases among men and 7.1 million cases among women. This was however doubled in 2010, with prevalence increasing to 4.0% (2.7, 6.4) and number of people living with diabetes reaching 24.5 million in both sexes, 11.3 million cases among men and 13.2 million cases among women (see **Tables 3.21, 3.22,** and **3.23,** and **Figures 3.21, 3.22,** and **3.23**).

Table 3.21. Prevalence and cases of diabetes in Africa in both sexes (estimates derived from epidemiological model and UN population demographics)

Age (years)	*1990*		*2000*		*2010*	
	$y = 0.289e^{0.0505x}$	Diabetes cases (000)	$y = 0.5542e^{0.0361x}$	Diabetes cases (000)	$y = 0.798e^{0.04x}$	Diabetes cases (000)
15-19	0.7	450	1.3	1138	1.6	1705
20-24	0.9	482	1.5	1143	1.9	1855
25-29	1.1	520	1.8	1119	2.3	1961
30-34	1.5	559	2.2	1107	2.9	1961
35-39	1.9	594	2.6	1118	3.5	1934
40-44	2.4	629	3.2	1122	4.3	1941
45-49	3.1	669	3.8	1105	5.2	1994
50-54	4.0	723	4.5	1070	6.4	2019
55-59	5.1	777	5.4	1025	7.8	1980
60-64	6.6	790	6.5	977	9.5	1868
65-69	8.5	749	7.8	896	11.6	1677
70-74	11.0	641	9.3	728	14.2	1442
75-79	14.1	469	11.2	510	17.4	1097
80+	21.7	453	15.2	446	24.4	1100
Total 15+ (95% CI)	2.4 (0.9, 4.1)	8 503	2.9 (1.7, 3.9)	13 505	4.0 (2.7, 6.4)	24 534

Table 3.22. Prevalence and cases of diabetes in Africa among men (estimates derived from epidemiological model and UN population demographics)

Age (years)	*1990*		*2000*		*2010*	
	$y = 0.2307e^{0.0496x}$	Diabetes cases (000)	$y = 0.2148e^{0.0524x}$	Diabetes cases (000)	$y = 0.6403e^{0.0424x}$	Diabetes cases (000)
15-19	0.8	256	0.8	343	1.4	764
20-24	1.0	271	1.0	373	1.7	837
25-29	1.3	290	1.3	395	2.1	891
30-34	1.6	309	1.7	422	2.6	903
35-39	2.1	327	2.2	462	3.3	902
40-44	2.7	343	2.8	498	4.0	911
45-49	3.4	360	3.7	530	5.0	938
50-54	4.4	383	4.8	552	6.2	947
55-59	5.6	405	6.2	564	7.6	933
60-64	7.2	404	8.1	574	9.4	875
65-69	9.2	372	10.5	562	11.7	776
70-74	11.8	310	13.7	483	14.4	658
75-79	15.1	218	17.8	356	17.8	490
80+	23.0	190	27.8	334	25.5	464
Total 15+	2.6 (0.4,3.8)	4 438	2.8 (1.4, 3.3)	6 449	3.8 (2.2, 5.9)	11 289

Table 3.23. Prevalence and cases of diabetes in Africa among women (estimates derived from epidemiological model and UN population demographics)

Age (years)	*1990*		*2000*		*2010*	
	$y = 0.1174e^{0.06x}$	Diabetes cases (000)	$y = 0.6243e^{0.0329x}$	Diabetes cases (000)	$y = 0.4617e^{0.0504x}$	Diabetes cases (000)
15-19	0.4	143	1.4	635	1.3	649
20-24	0.6	161	1.7	629	1.7	732
25-29	0.8	183	2.0	607	2.2	780
30-34	1.1	207	2.4	594	2.8	814
35-39	1.4	231	2.8	592	3.6	866
40-44	2.0	257	3.3	590	4.7	941
45-49	2.6	291	3.9	573	6.0	1025
50-54	3.6	332	4.6	552	7.7	1081
55-59	4.8	378	5.4	528	9.9	1120
60-64	6.5	409	6.3	503	12.8	1138
65-69	8.8	415	7.5	460	16.4	1133
70-74	11.8	380	8.8	376	21.2	1047
75-79	16.0	300	10.4	266	27.2	829
80+	26.6	336	13.7	238	41.8	1126
Total 15+	2.3 (0.2, 3.2)	4 073	3.0 (1.8, 4.2)	7 144	4.9 (2.9, 7.1)	13 230

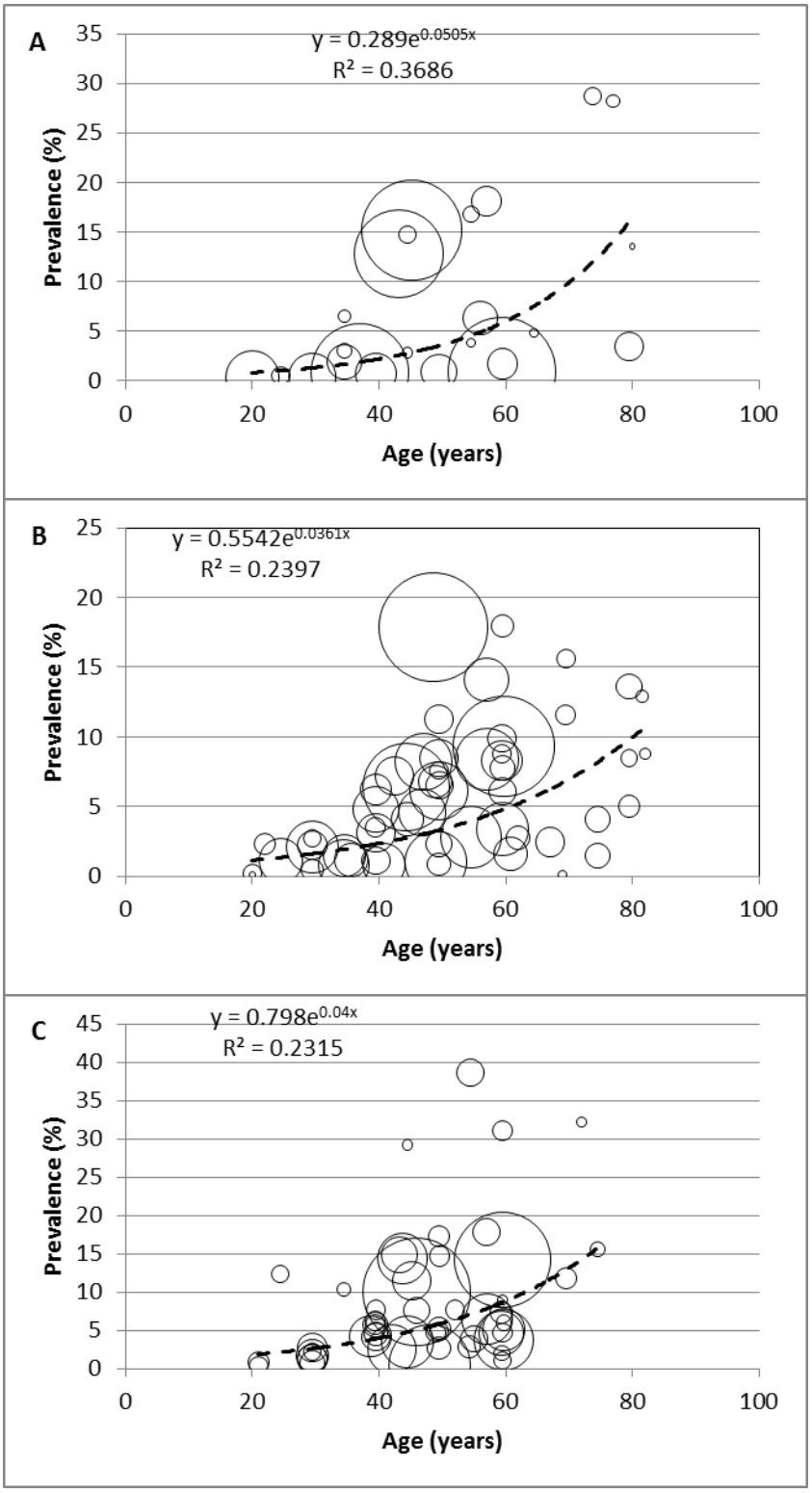

Figure 3.21. Epidemiological model showing relationship between age and crude prevalence of diabetes in both sexes in Africa, with size of bubble corresponding to sample size (A: 1990, B: 2000, C: 2010)

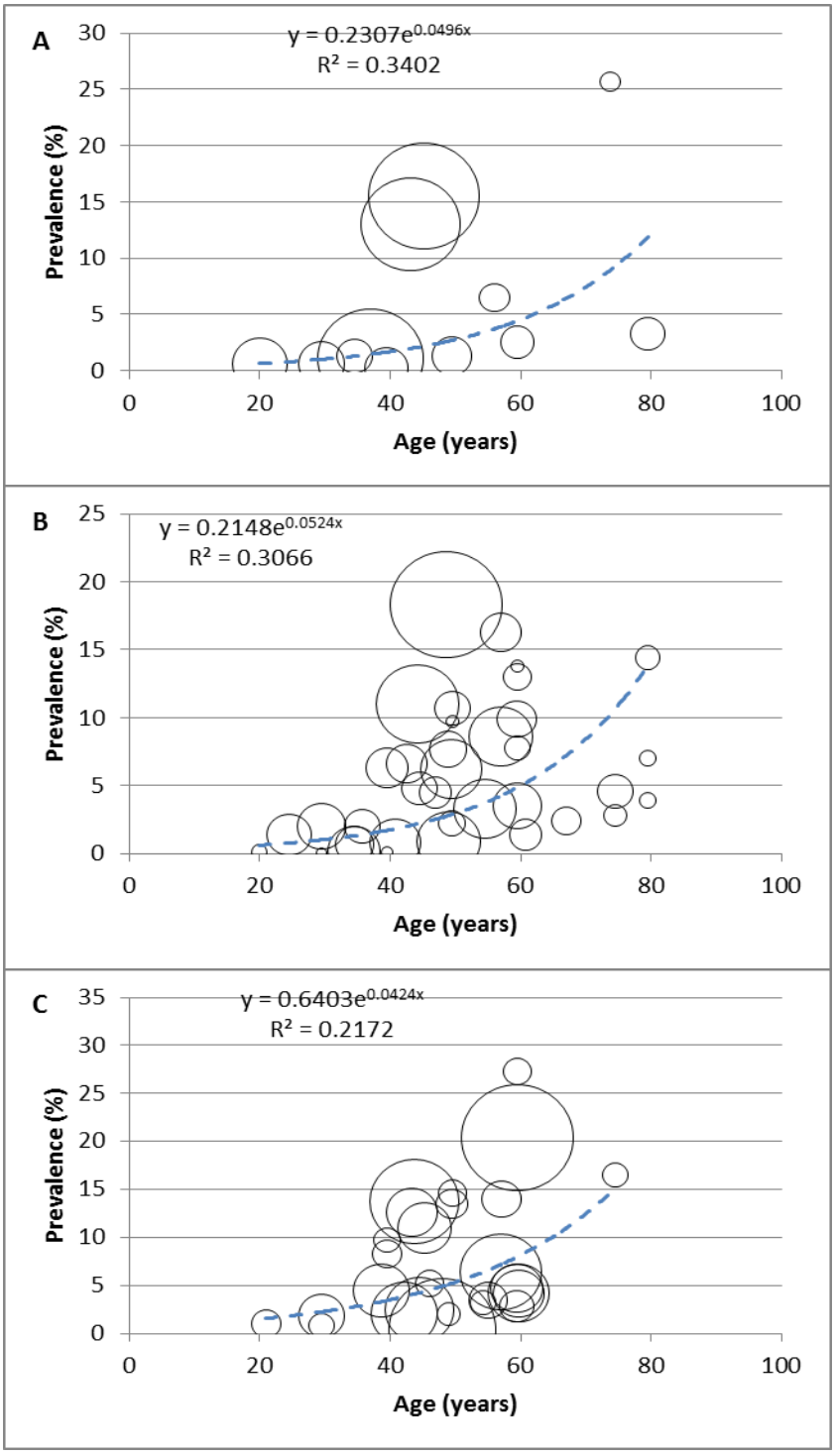

Figure 3.22. Epidemiological model showing relationship between age and crude prevalence of diabetes among men in Africa, with size of bubble corresponding to sample size (A: 1990, B: 2000, C: 2010)

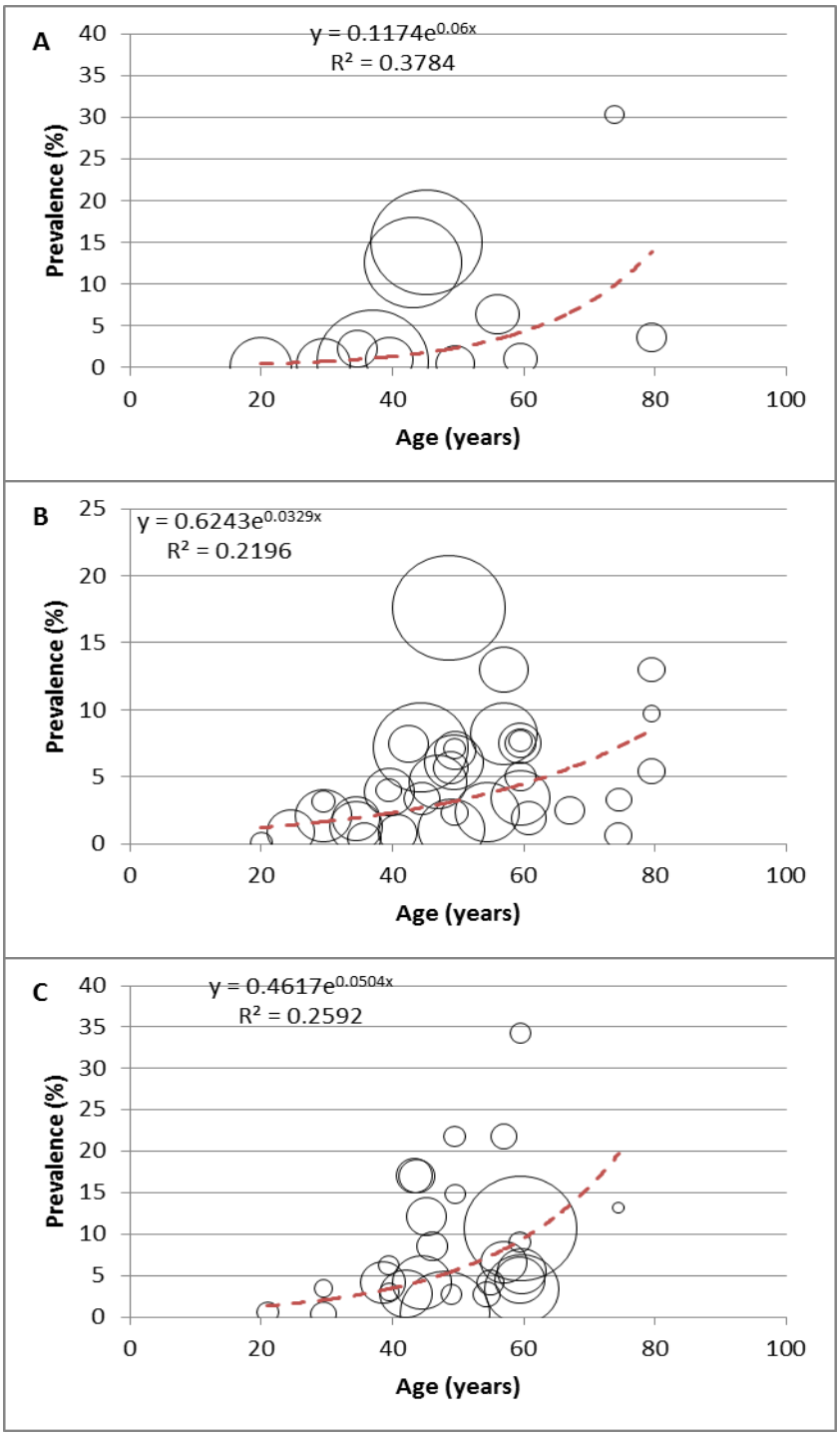

Figure 3.23. Epidemiological model showing relationship between age and crude prevalence of diabetes among women in Africa, with size of bubble corresponding to sample size (A: 1990, B: 2000, C: 2010)

3.4 CANCER

Systematic review

The literature search returned 9762 publications identified from three databases: Medline (3437), EMBASE (4604) and Global Health (1721). A further 4 studies were selected from other sources, which included studies identified from Google Scholar, the "GLOBOCAN studies", "Cancer Incidence in Five Continents (CI5) series", and "Cancer in Africa: Epidemiology and Prevention"). No further studies were identified from additional searches of websites of International Association of Cancer Registries (IACR), International Agency for Research on Cancer (IARC), and WHO African region, as I could not access these data. However, some of the global cancer publications noted above reported data from these registries, which were extracted. After all studies have been collated and duplicates removed, 6108 records remained. On screening titles for relevance (cancer studies conducted primarily on African populations), 5806 studies were excluded, giving a total of 302 full texts that were assessed. After applying the quality criteria, 263 studies were excluded (134 articles did not provide numerical estimates on incidence of cancers, and 129 articles did not clarify cancer registration process). A total of 39 studies (33 included for meta-analysis) were finally retained for the review (**Figure 3.24).** The relative lower number of studies retained (compared to the initial output of 9762) was because most of the studies screened were not reporting incidence rates of cancer or comparable figures from which incidence rates may be estimated.

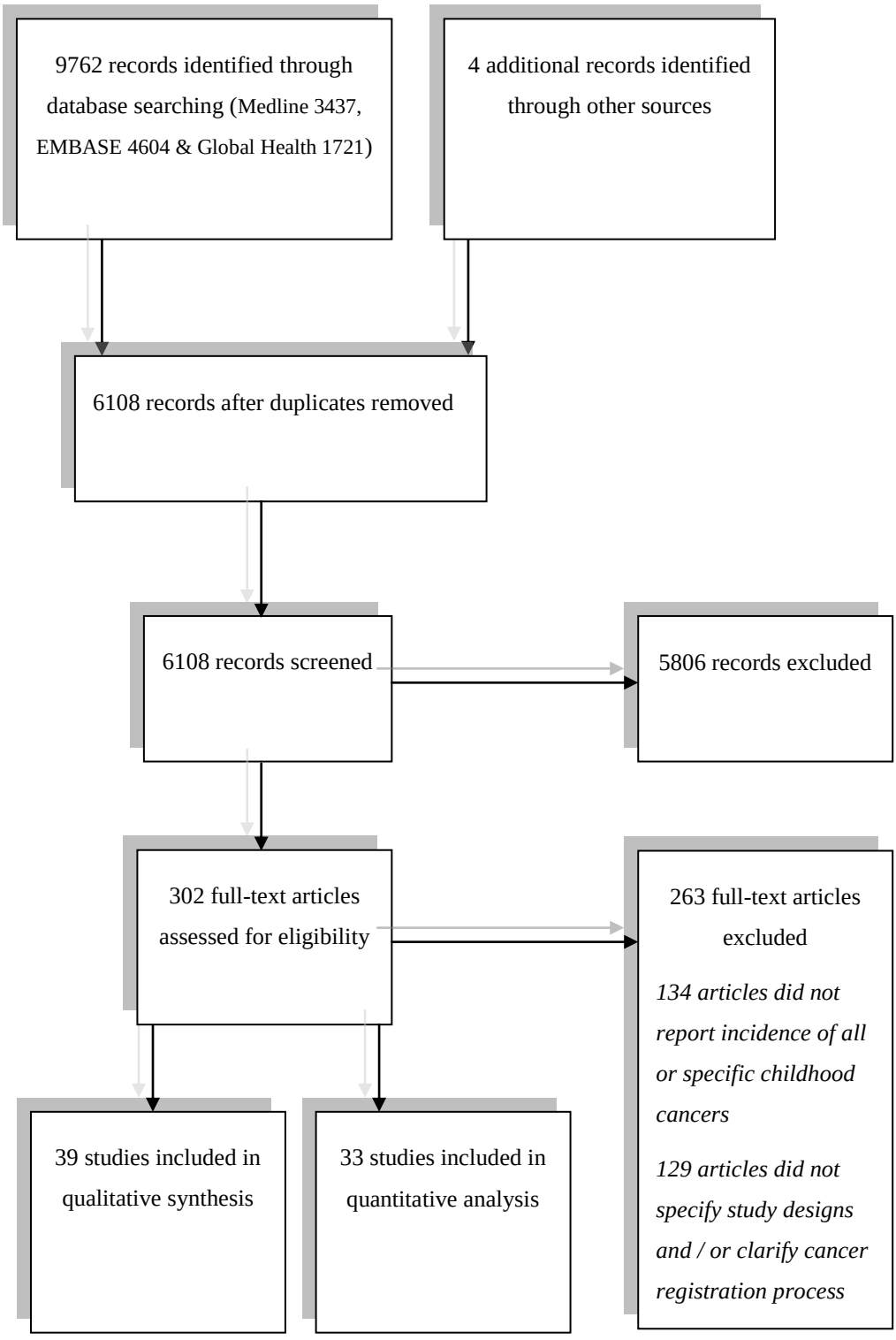

Figure 3.24. Flow diagram of search results for cancer studies in Africa

Study characteristics

The retained 39 studies were conducted across 20 African countries, with Egypt and South Africa highest having highest number of studies (5 studies each) (**Table 3.24**). Across African regions, Central Africa had 3 studies conducted in 3 African countries, Eastern Africa had 5 studies conducted in 3 African countries, Northern Africa had 11 studies conducted in 4 African countries, Southern Africa had 11 studies conducted in 5 African countries, and Western Africa had 9 studies conducted in 5 African countries (**Figure 3.25**).

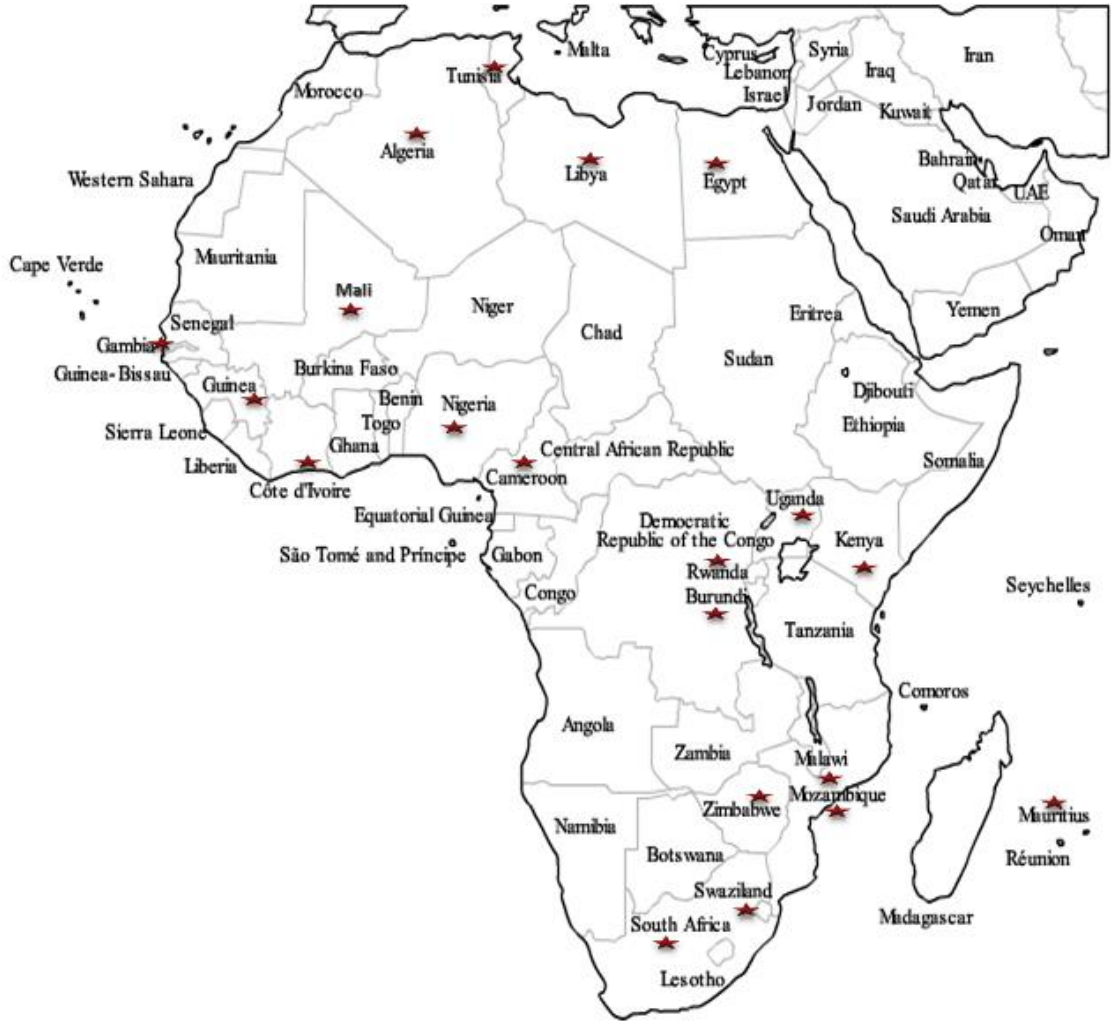

Figure 3.25. Map of Africa with asterisks showing countries of the retained cancer studies

Of the 39 studies, data from 36 studies were collated from 27 population-based cancer registries, which do not necessarily cover an entire country population; some only cover provinces, districts or major cities within the country. 3 studies were based on cross sectional population-based surveys (Kocheleff et al., 1984, Menendez et al., 2010, Fonn et al., 2002). Periods of studies range from 1 year to 13 years with a median study period of 5 years. The cancer registries in the retained studies cover a population of about 33 million. Cancer registrations comply with the ICD-O or the ICD coding system, with studies mainly using the ICD-O (1-3) and the ICD (9 & 10). Few studies reported methods of confirming cancer diagnosis, mainly through morphological/ histological verification, death certificates only (DCO) or active/ passive case finding (**Table 3.25).**

Table 3.24. Characteristic distribution of retained cancer studies in Africa

Characteristics	***Country***	***Study sites***
Central Africa (3 study sites)	Burundi	1
	Cameroon	1
	Rwanda	1
Eastern Africa (5 study sites)	Kenya	2
	Mauritius	1
	Uganda	2
Northern Africa (11 study sites)	Algeria	1
	Egypt	5
	Libya	2
	Tunisia	3
Southern Africa (11 study sites)	Malawi	1
	Mozambique	1
	South Africa	5
	Swaziland	1
	Zimbabwe	3
Western Africa (9 study sites)	Cote d'Ivoire	1
	Gambia	3
	Guinea	1
	Mali	1
	Nigeria	3
Duration of study		
<1 year		7
1-3 years		11
>3 years		21
Study methods		
Registry-based		36
Population-based		3

Table 3.25. Overall characteristics of retained studies reporting incidence rates of cancer in Africa

African Region	*Country, Location/ Registry*	*Study period*	*Total study population*	*Diagnostic criteria*	*Confirmation of diagnosis (%)*
Central	1) Burundi** (Kocheleff et al., 1984)	1983-1984	851,412	Alpha Feto Protein (AFP) Screening to detect liver cancer	AFP
	2) Cameroon, Yaounde (Enow Orock et al., 2012)	2004–2006/ 2010–2011	1,299,369	CanReg5	Morphologically verified (89%)
	3) Rwanda, Butare (Newton et al., 1996)	1991-1994	-	ICD-9	-
East	4) Kenya, Eldoret* (Tenge et al., 2009)	1999-2006	1,400,000	Cases are identified from the disease index (completed by records staff in ICD-10) and details of cases abstracted from case records	-
	5) Kenya, Greater Meru (McFarlane et al., 2001)	1991-1993	1,144,594	ICD-10	-
	6) Mauritius (Manraj et al., 1998)	1989-1993	1,035,806	ICD	-
	7) Uganda, Kampala (Parkin et al., 2010)	1991-2006	1,674,384	ICD-O-2	-
	8) Uganda, Kyadondo (Wabinga et al., 2000)	1990-1997	-	ICD-O (Percy et al. 1990); ICD-10 for tabulation	Morphologically verified (64%)
North	9) Algeria, Setif* (Hamdi Cherif et al., 2010)	1986-2005	-	CanReg4	-
	10) Egypt, Menofeia (Soliman et al., 1999)	1992-1996	2,755,000	SEER and combined diagnoses by tumor site according to the ICD-9 code	-
	11) Egypt, Nile Delta (Fedewa et al., 2009)	1999-2002	-	CanReg- Poisson regression; ICD-9	Microscopy (90.8%)
	12) Egypt (Dey et al., 2010)	1999-2002	-	ICD-9	-
	13) Egypt, Alexandria (Abdel-Fattah and Yassine, 2007)	1995-2004	-	ICD-10	-

	14) Egypt, Gharbiah (Lehman et al., 2008)	1999–2003	4,200,000	ICD-10, ICD-O-3	-
	15) Libya, Benghazi (El Mistiri et al., 2007)	2003	660,147	ICD-O-3	Microscopically / histologically verified (79%)
	16) Libya, Eastern region (El Mistiri et al., 2010)	2004	-	ICD-10	-
	17) Tunisia, Souse (Missaoui et al., 2010)	1993-2006	2,760,900	ICD-10	Morphologically verified (97%)
	18) Tunisia, North-eastern (Ben Abdallah et al., 2009)	1994-1998	-	Can Reg, ICD 9	-
	19) Tunisia, Central (Missaoui et al., 2012)	1993-2007	-	ICD-10, ICD-O	-
South	20) Malawi, Blantyre (Banda et al., 2001)	1994-98	782,000	Histopathology, ultrasound and endoscopy, radiography, biochemical tests (AFP). ICD-O-2 used for data entry, but converted to ICD-10 for tabulation and morphology	Morphological (histological/cytological) verification (39%)
	21) Mozambique, Manhica** (Menendez et al., 2010)	2000	36,000	ICD-9	-
	22) South Africa (Somdyala et al., 2003)	1991-1995	-	Data were computerised and coded at the time of entry, following the tumour nomenclature and coding for topography	Active and Passive methods of case finding
	23) South Africa, Eastern Cape (Somdyala et al., 2010)	1998-2002	1,292,959	ICD-10, ICD-O	Histologically verified (42.8%)
	24) South Africa, Johannesburgh (Mqoqi, 2004)	1998-1999	-	ICD-9, ICD-O	Active case finding
	25) South Africa** (Fonn et al., 2002)	2002	20603	ICD- 9	-
	26) South Africa, Northern Cape (Wentink et al., 2010)	2002-2009	1,102,200	ICD-10, ICD-O	-
	27) Swaziland (Parkin et al., 2008)	1996-1999	-	ICD-O	-

	28) Zimbabwe, Harare (Chokunonga et al., 2000)	1993-1995	-	ICD-O, converted to ICD-10 for analysis	Histologically verified (62.2%)
	29) Zimbabwe, Harare (Bassett et al., 1995)	1990-1992	-	ICD-O, ICD-10	Death certificates only (DCO)
	30) Zimbabwe (Marimo and Hille, 2006)	1988-1997	1,412,548	ICD 10	-
West	31) Cote d'Ivoire, Abidjan (Echimane et al., 2000)	1995-1997	1,000,342	Histopathology- coded using ICD-0 2nd edition, converted to ICD-10 for tabulation	Morphologic verification (81.1%)
	32) Gambia (Bah et al., 2001)	1988-1997	1,340,000	ICD-0, ICD 10	Histologically verified (21.0%)
	33) Gambia (Sighoko et al., 2011)	1998–2006		ICD-10, ICD-O-3	-
	34) Gambia* (Sighoko et al., 2010)	1998-2006	1,310,681	CanReg 4	-
	35) Guinea, Conakry (Koulibaly et al., 1997)	1992-1995	6,700,000	Tumor site and histology have been coded using the ICD-0 first edition (WHO, 1976). These codes were converted to ICD-9 for tabulation (although cases of Kaposi's sarcoma were given a separate category.	Morphologically verified (26.7%)
	36) Mali, Bamako (Bayo et al., 1990)	1987-1988	646,163	ICD-O (WHO 1976), ICD-9 (Percy & Van Holten, 1979)	Death certificate only (DCO)
	37) Nigeria, Ibadan & Abuja (Jedy-Agba et al., 2012)	2009-2010	3,955,504	ICD-O-3	-
	38) Nigeria, Maiduguri (Nggada et al., 2008)	2001-2005	-	ICD	-
	39) Nigeria (Ogunbiyi and Shittu, 1999)	1980-1996	-	ICD-9	-

**not included in meta-analysis, **population-based study, ICD: International Classification of Diseases, ICD-O: International Classification of Diseases for Oncology*

Details of quality criteria and grading of retained cancer studies in Africa

Of the retained 39 studies, three studies were graded low quality (**Table 3.26**). These studies, despite having well explained study designs were not included in the meta-analysis due to incomplete data needed for the estimation of incidence of cancer. There were 3 other studies graded as medium quality, however, they were not included in that meta-analysis as these were mainly cross-sectional population based studies. All data included in the meta-analysis were from population/hospital-based cancer registries.

Table 3.26. Quality assessment of retained cancer studies in Africa

Study ID*	***Study design***	***Study analysis***	***Study limitations***	***Generalizability to Africa***	***Grading***
2, 3, 5-8, 10-20, 22-24, 26-33, 35-39	Well explained across all studies	Well explained across all studies	Well-presented across all studies	Study population representative of a larger African population	*High*
1, 21, 25	Well explained across all studies	Not well explained	Not well-presented	Study population representative of a larger African population in the three studies	*Moderate*
4, 9, 34	Well explained	Not well explained	Not well presented	Study population not fairly representative of a larger African population	*Low*

see **Table 3.25 for details of Study ID*

Pooled incidence rates of major cancers in Africa

From the 36 studies conducted on population-based cancer registries, 3 studies had incomplete data and or without denominators from which incidence rates can be estimated. 33 studies were therefore included in the meta-analysis, with specific cancer incidence rates estimated for men and women. Among women, the top five cancers were cancers of the cervix, breast, Kaposi, liver and colorectal, while cancers of the prostate, Kaposi, oesophagus, liver and lungs were the top five cancers among men (**Table 3.27**). The reported crude incidence rates were not modelled as many studies did not report age-specific incidence rates of cancers. All reported crude incidence rates are estimated per 100,000person years.

Table 3.27. Overall summary of pooled incidence rates of major cancers in Africa

Cancer site	*Incidence per 100,000 person years*		*Heterogeneities (I^2 (%))*		*Estimated new cancer cases in 2010†*	
	Male (95% CI)	Female (95% CI)	Male	Female	Male	Female
Kaposi	14.3 (11.9, 16.7)	6.5 (5.2, 7.8)	99.0	95.3	73668	29743
Liver	12.6 (10.0, 15.3)	5.7 (4.4, 7.0)	97.8	95.3	64910	26042
Colorectal	5.3 (4.0, 6.5)	3.9 (2.9, 4.9)	93.6	94.0	27098	17864
Stomach	5.6 (4.2, 7.1)	3.8 (2.9, 4.6)	95.0	95.6	29004	17362
Lung	9.3 (6.8, 11.7)	1.9 (1.3, 2.5)	97.5	90.8	47704	8772
NHL	3.9 (2.8, 5.0)	2.9 (2.1, 3.7)	94.1	93.6	20143	13113
Oesophagus	13.4 (10.2, 16.6)	-	98.8	-	69032	-
Bladder	5.8 (4.2, 7.4)	-	95.9	-	29879	-
Cervix	28.2 (22.1, 34.4)		99.0		128841	
Breast	17.7 (13.0, 22.4)		99.1		80868	
Ovary	3.6 (2.7, 4.4)		89.0		16448	
Prostate	14.5 (10.9, 18.0)		98.8		74698	

†estimated cases based on pooled incidence rates, NHL: non-Hodgkins lymphoma

3.4.1 Cervical cancer

There were 24 data points from 16 African countries with a pooled incidence rate of 28.230/100,000 (22.056, 34.404), I^2 = 99.0%, p = 0.000 (**Figure 3.26**). In 2010, this would amount to about 129,000 new cases of cervical cancer in Africa.

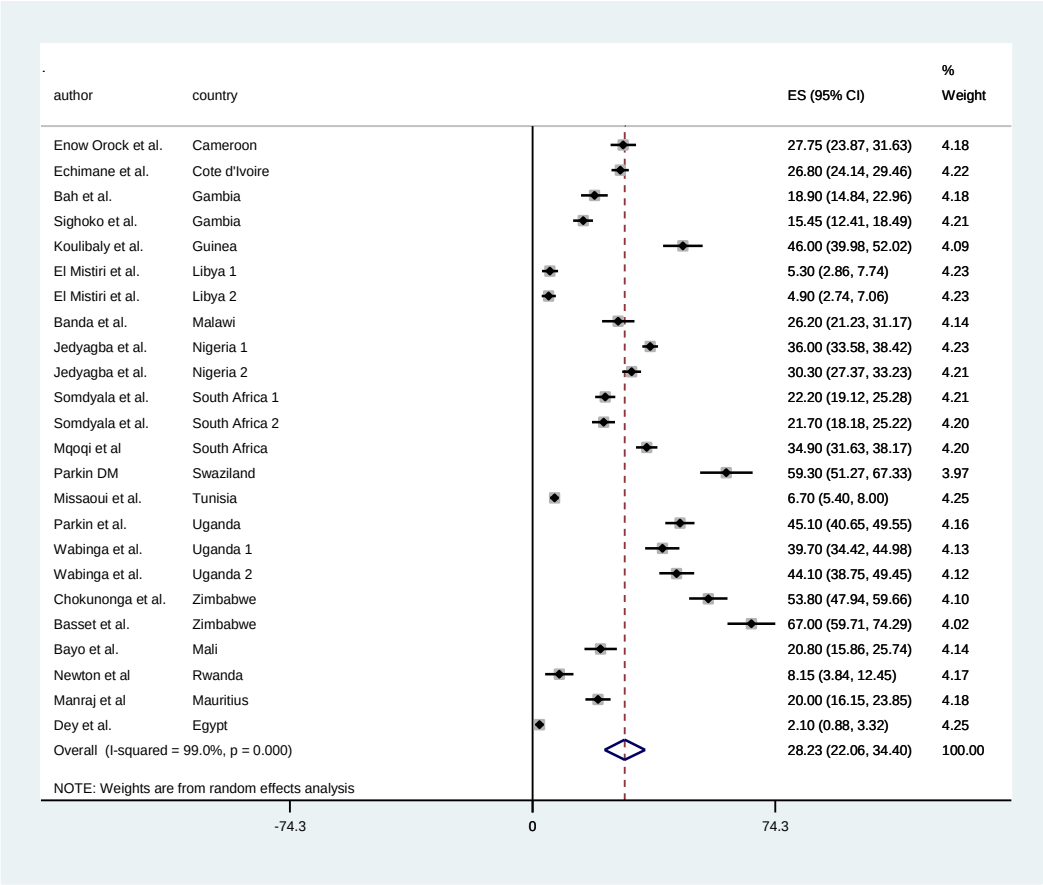

Figure 3.26. Forest plot showing pooled incidence rate of cervical cancer in Africa

3.4.2 Breast cancer

There were 26 data points from 17 African countries with a pooled incidence rate of 17.727/100,000 (13.016, 22.438), I^2= 99.1%, p = 0.000 (**Figure 3.27**). In 2010, this would amount to about 81 thousand new cases of breast cancer among women in Africa.

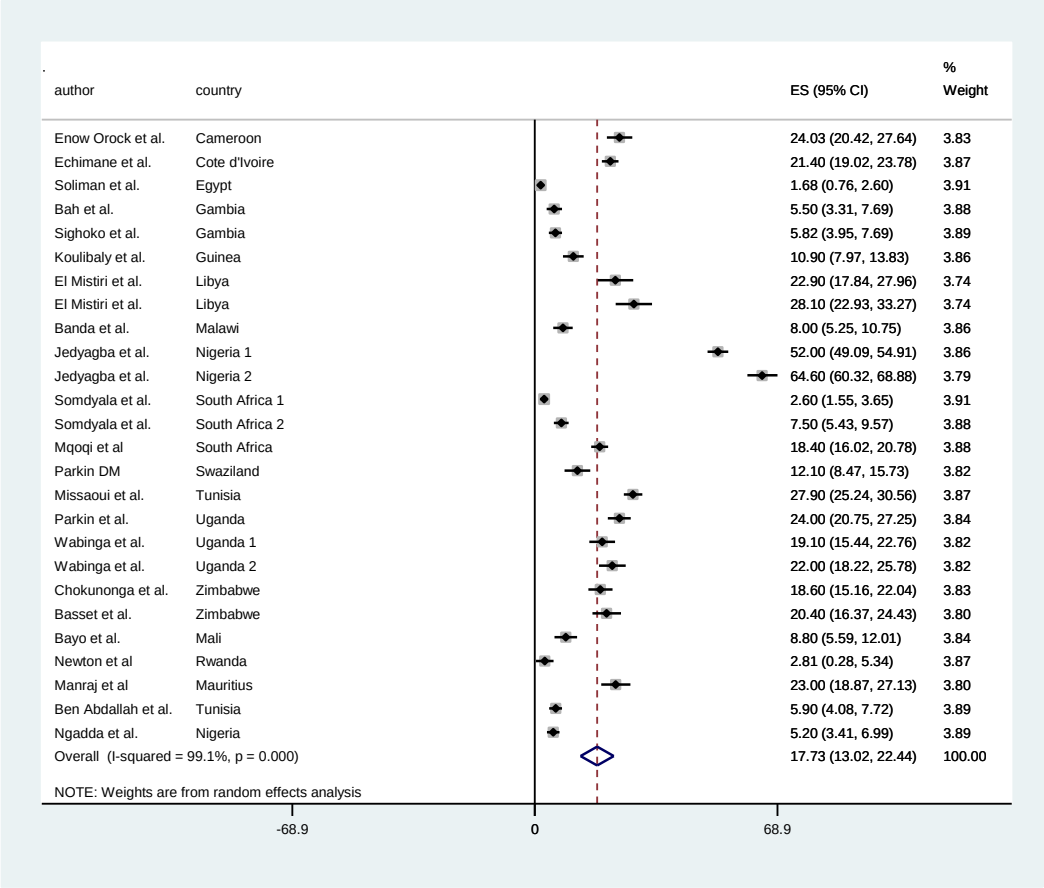

Figure 3.27. Forest plot showing pooled incidence rate of female breast cancer in Africa

3.4.3 Ovarian cancer

There were 21 data points from 15 African countries with a pooled incidence rate of 3.6/100,000 (2.7, 4.4), I^2 = 89.0%, p = 0.000 (**Figure 3.28**). In 2010, this would amount to over 16 thousand new cases of ovarian cancer in Africa

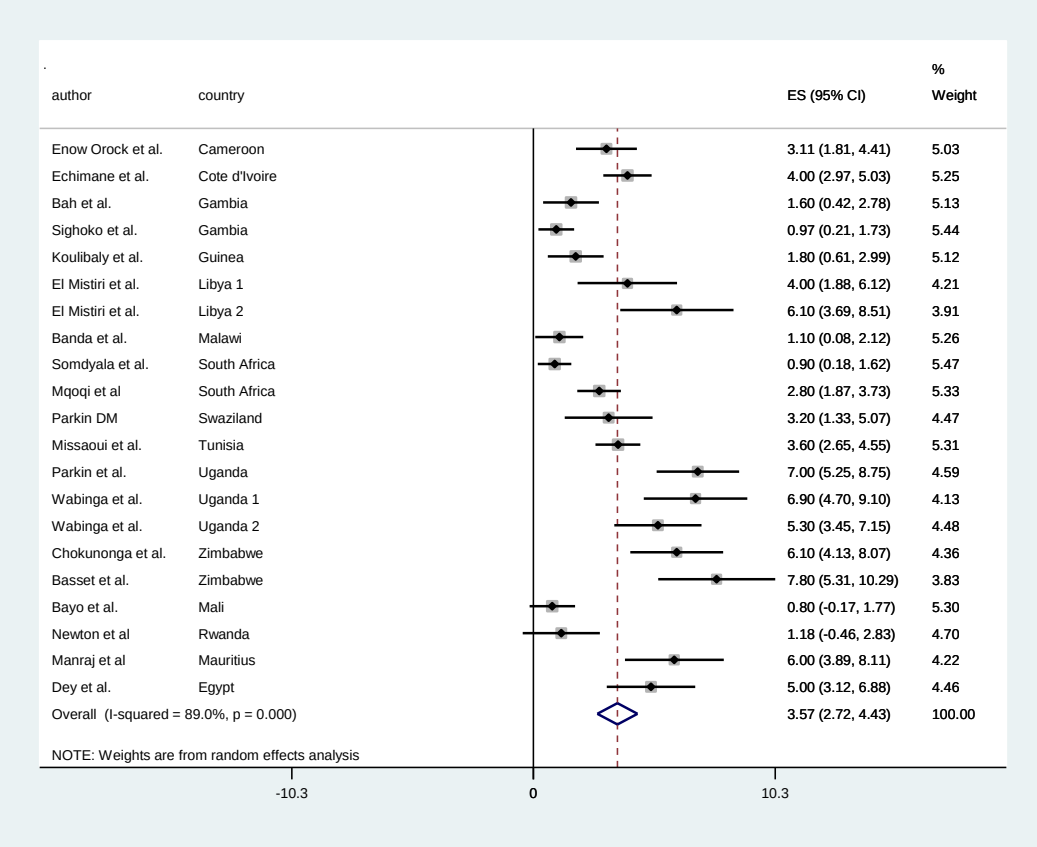

Figure 3.28. Forest plot showing pooled incidence rate of ovarian cancer in Africa

3.4.4 Prostate cancer

There were 24 data points from 16 African countries with a pooled incidence rate of 14.461/100,000 (10.949-17.972), I^2 = 98.8%, p = 0.000 (**Figure 3.29**). In 2010, this would amount to about 75 thousand new cases of prostate cancer in Africa.

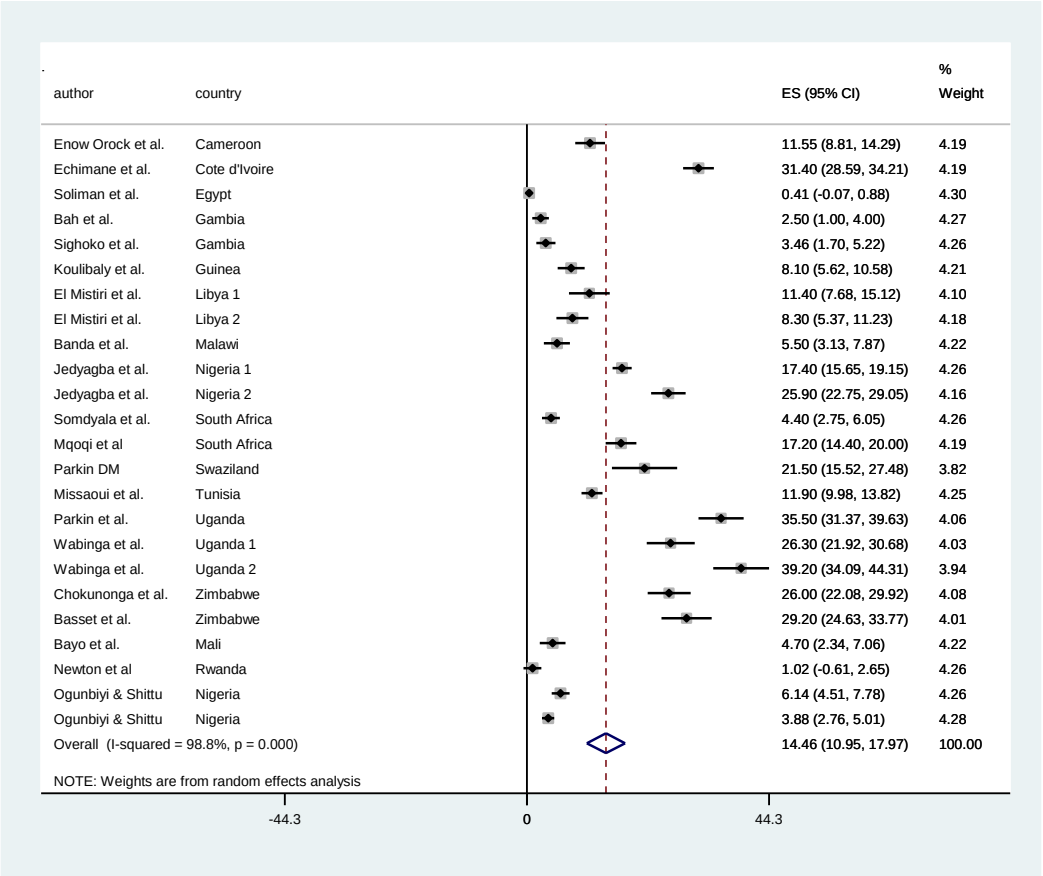

Figure 3.29. Forest plot showing pooled incidence rate of prostate cancer in Africa

3.4.5 Cancer of the Oesophagus

Men

There were 23 data points from 14 African countries with a pooled incidence rate of 13.39/100,000 (10.214, 16.575), I^2 = 98.8%, p = 0.000 (**Figure 3.30**). In 2010, this would amount to over 69 thousand new cases of cancer of the oesophagus among men in Africa,

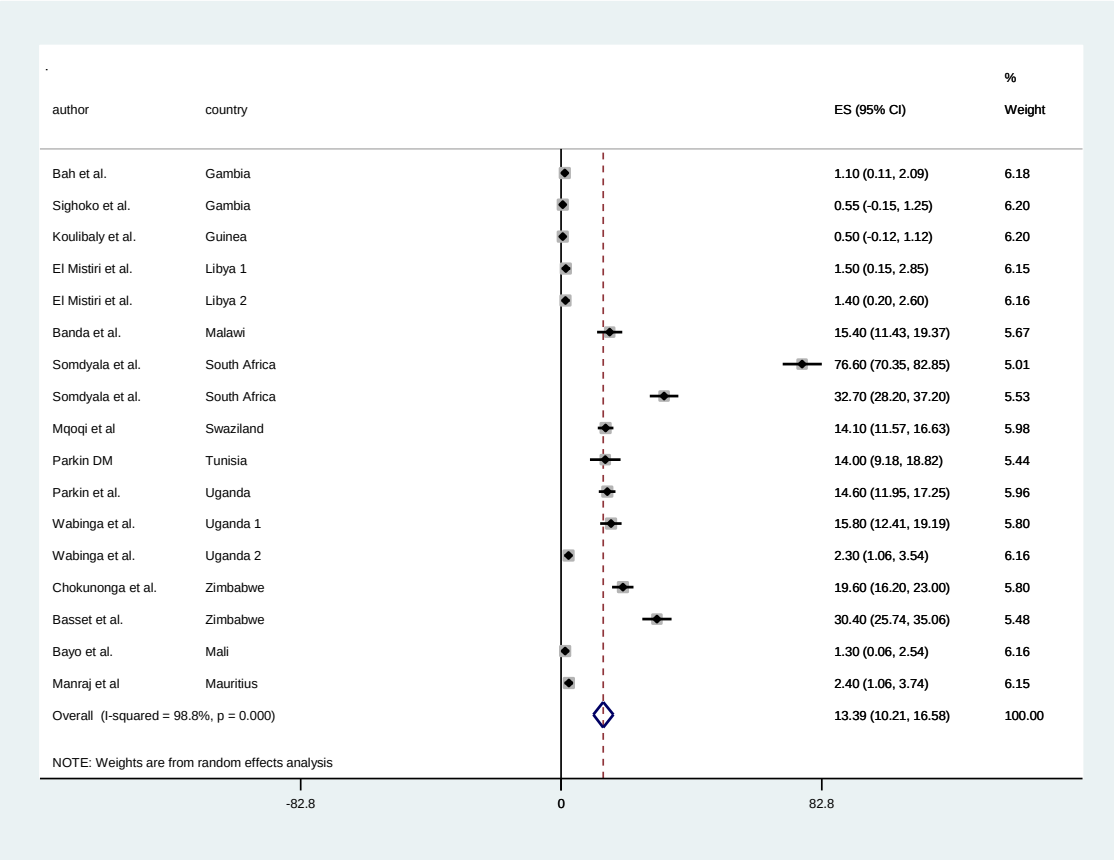

Figure 3.30. Forest plot showing pooled incidence rate of cancer of the oesophagus among men in Africa

3.4.6 Bladder Cancer

Men

There were 18 data points from 13 African countries with a pooled incidence rate of 5.821/100,000 (4.202, 7.440), I^2 = 95.9%, p = 0.000 (**Figure 3.31**). In 2010, this would amount to about 30 thousand new cases of bladder cancer among men in Africa.

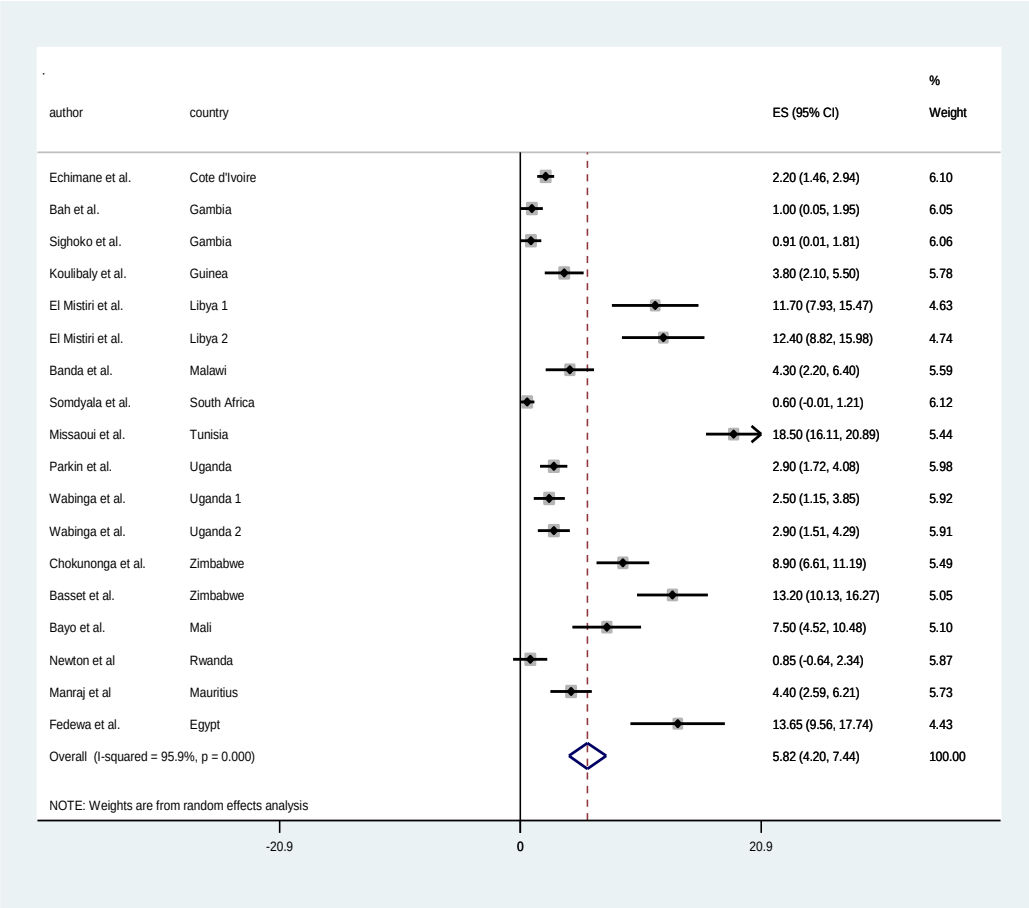

Figure 3.31. Forest plot showing pooled incidence rate of bladder cancer among men in Africa

3.4.7 Kaposi sarcoma

i. Men

There were 16 data points from 10 African countries with a pooled incidence rate of 14.297/100,000 (11.888-16.706), I^2= 99.0%, p = 0.000 (**Figure 3.32**). In 2010, this would amount to about 74 thousand new cases of Kaposi sarcoma among men in Africa.

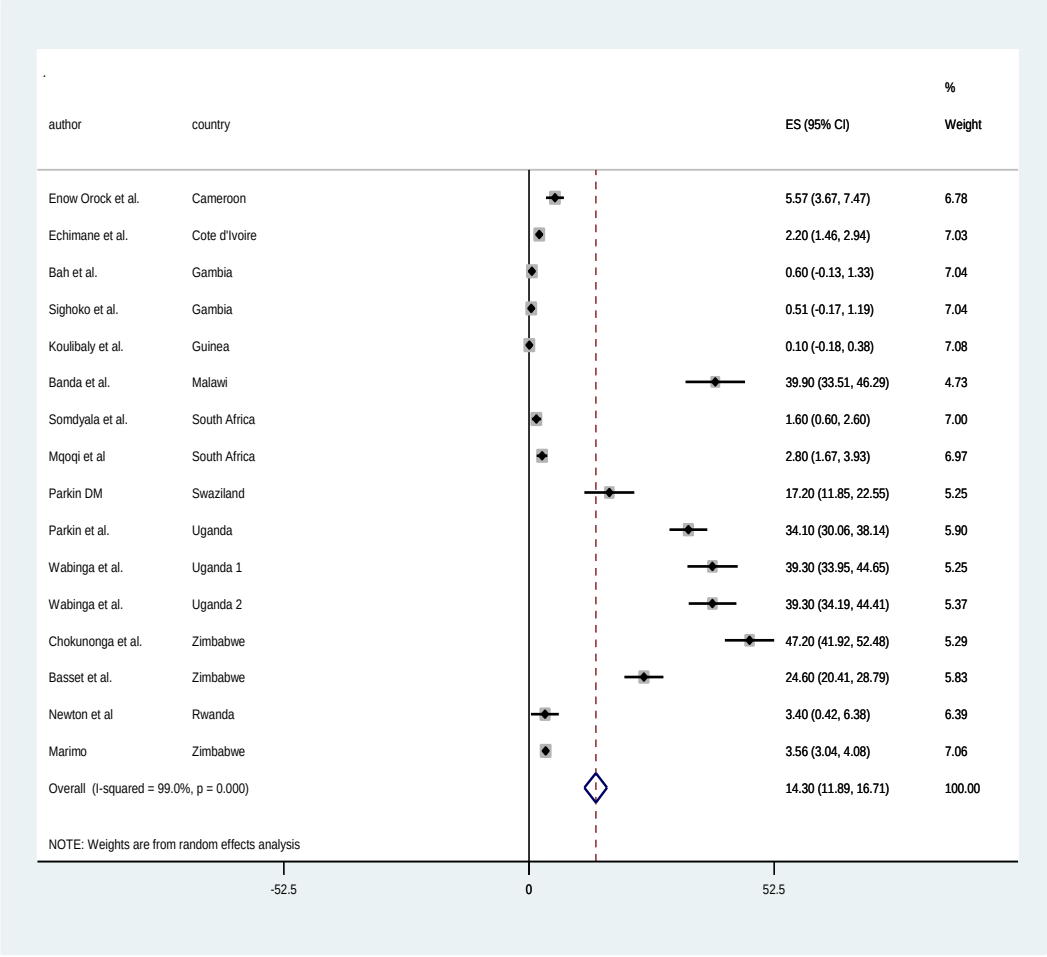

Figure 3.32. Forest plot showing pooled incidence rate of Kaposi sarcoma among men in Africa

ii. Women

There were 16 data points from 10 African countries with a pooled incidence rate of 6.514/100,000 (5.180, 7.849), I^2 = 95.3%, p = 0.000 (**Figure 3.33**). In 2010, this would amount to about 30 thousand new cases of Kaposi sarcoma among women in Africa.

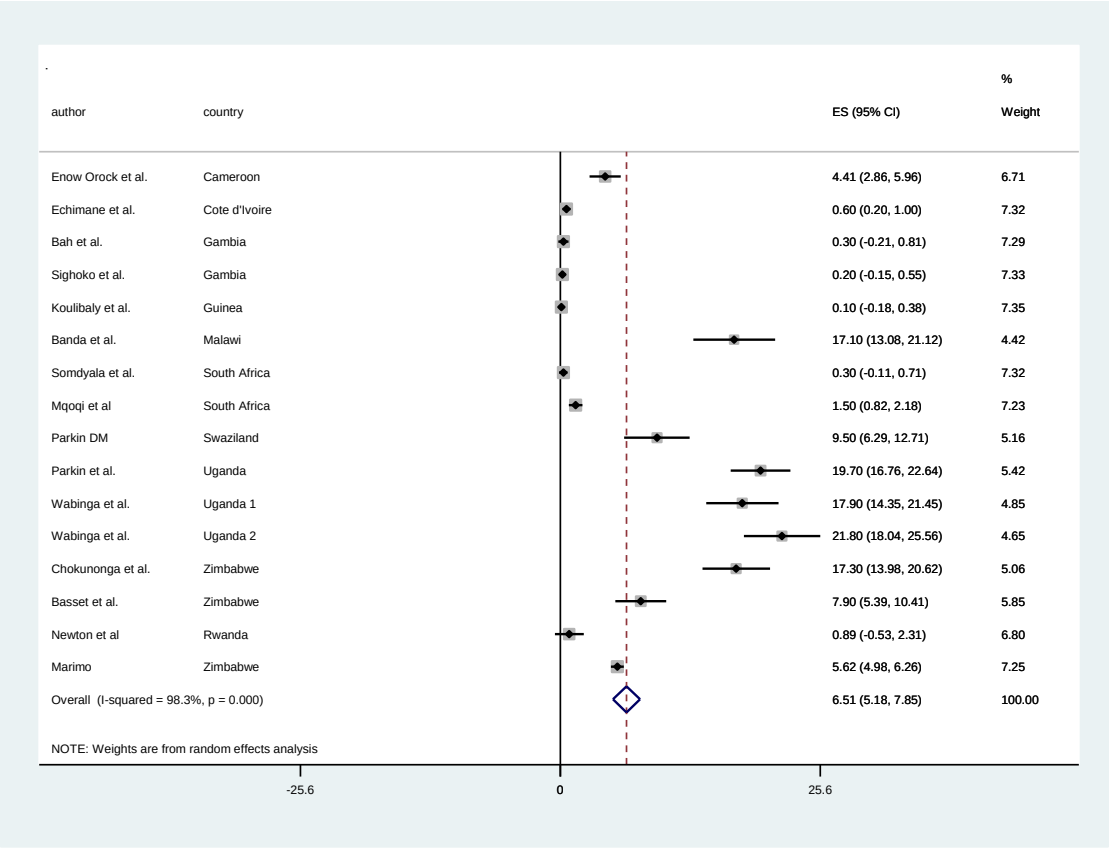

Figure 3.33. Forest plot showing pooled incidence rate of Kaposi sarcoma among women in Africa

3.4.8 Liver cancer

i. Men

There were 23 data points from 14 African countries with a pooled incidence rate of 12.631/100,000 (9.995, 15.268), I^2= 97.8%, p = 0.000 (**Figure 3.34**). In 2010, this would amount to about 65 thousand new cases of liver cancer among men in Africa.

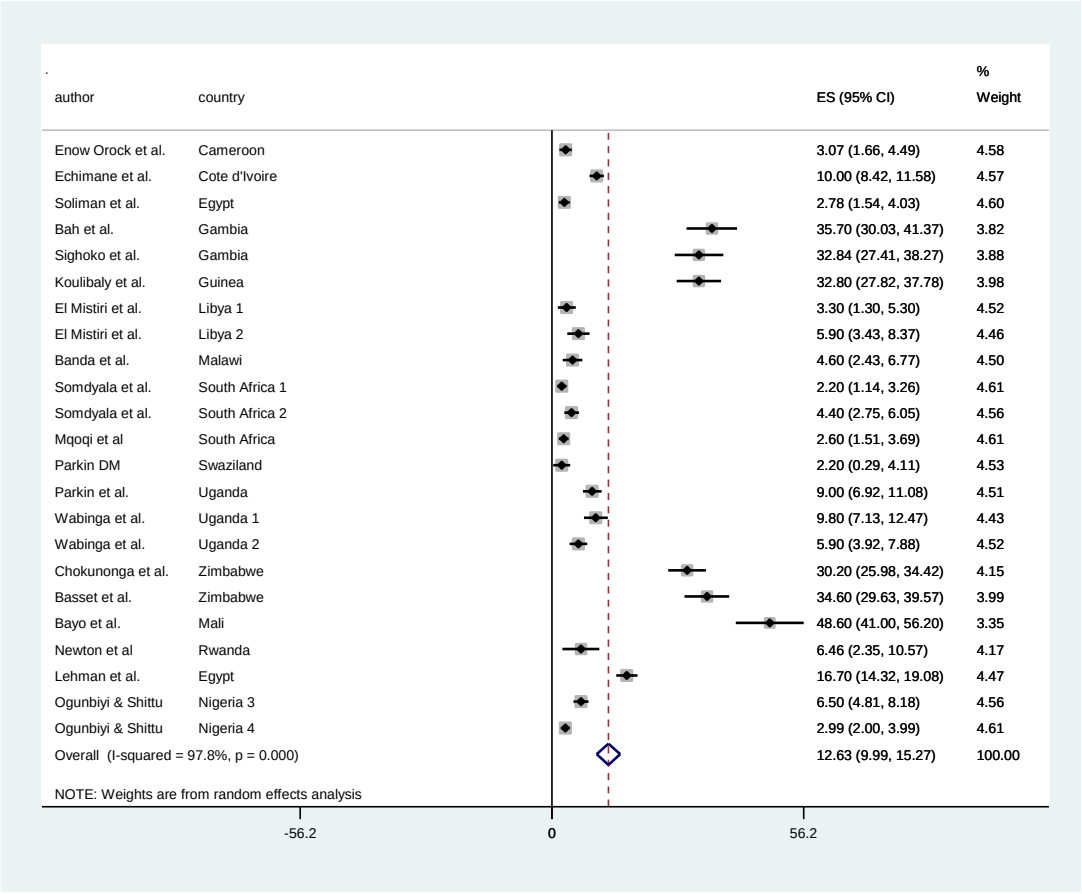

Figure 3.34. Forest plot showing pooled incidence rate of liver cancer among men in Africa

ii. *Women*

There were 21 data points from 14 African countries with a pooled incidence rate of 5.703/100,000 (4.380, 7.026), I^2= 95.3%, p = 0.000 (**Figure 3.35**). In 2010, this would amount to over 26 thousand new cases of liver cancer among women in Africa.

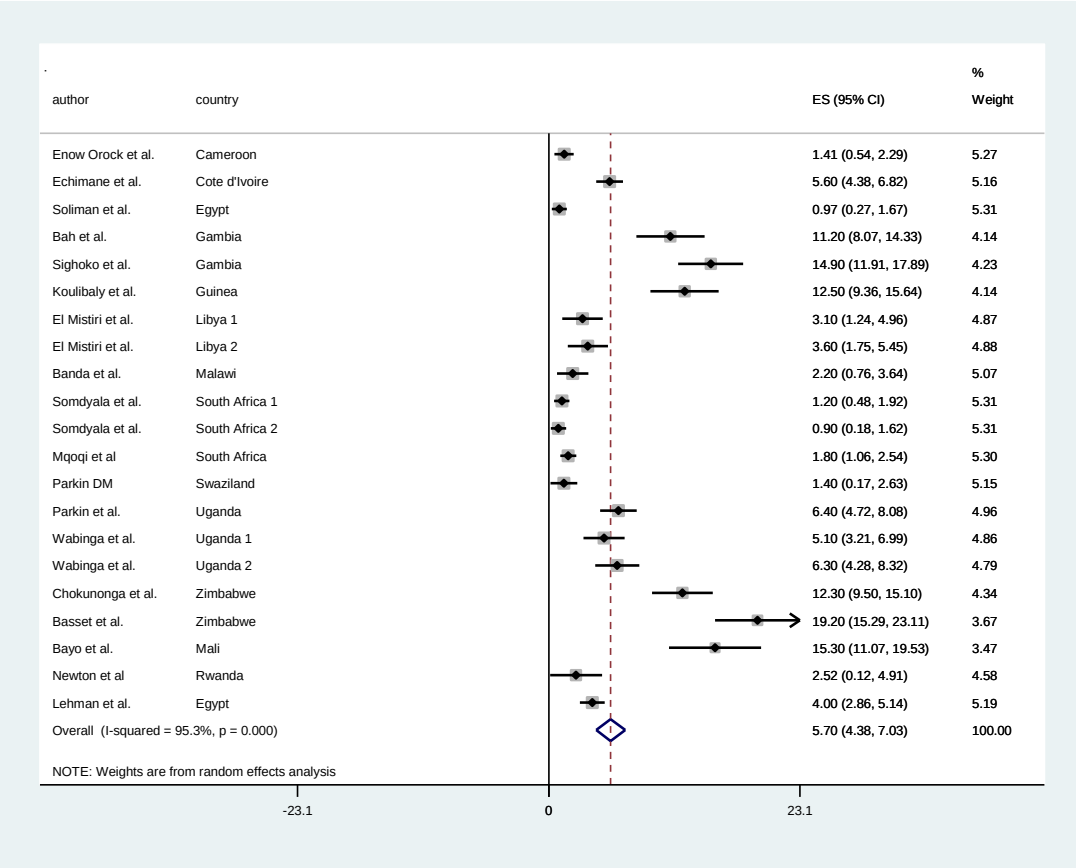

Figure 3.35. Forest plot showing pooled incidence rate of liver cancer among women in Africa

3.4.9 Lung cancer

i. Men

There were 20 data points from 14 African countries with a pooled incidence rate of 9.258/100,000 (6.784, 11.732), I^2 = 97.5%, p = 0.000 (**Figure 3.36**). In 2010, this would amount to about 48 thousand new cases of lungs cancer among men in Africa.

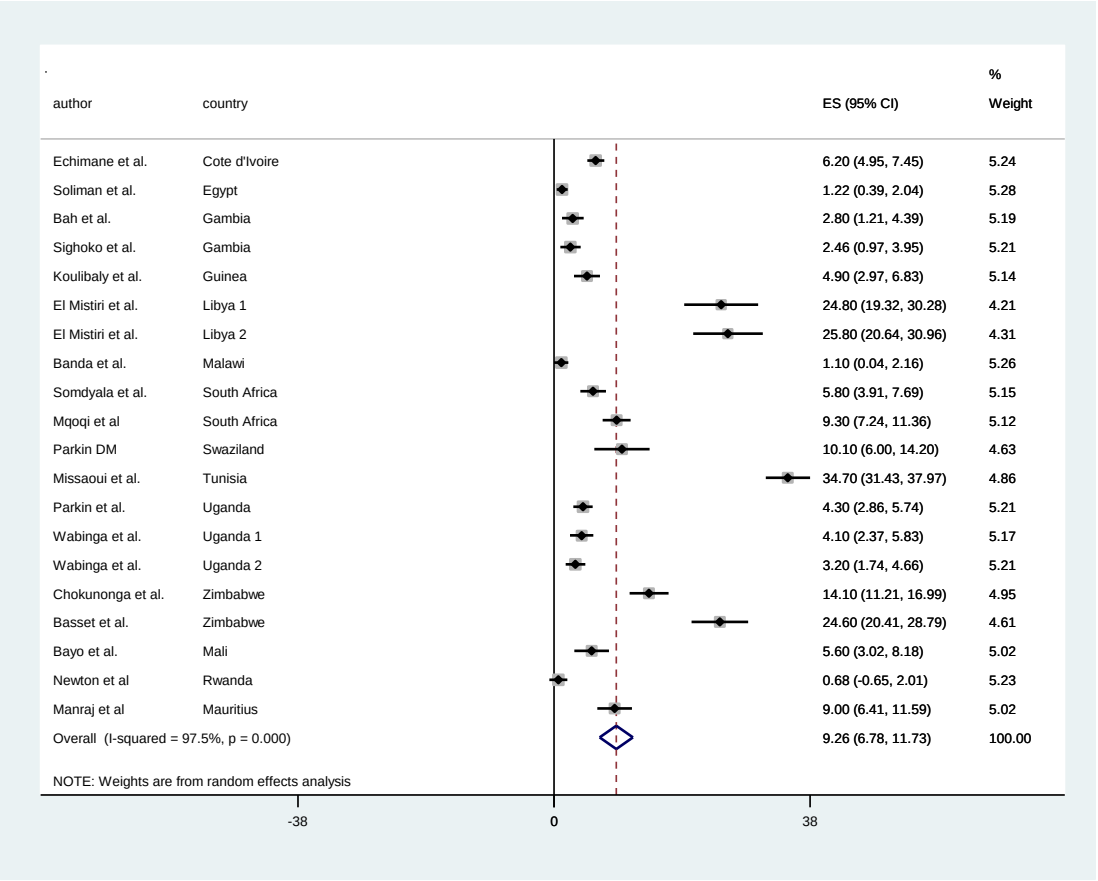

Figure 3.36. Forest plot showing pooled incidence rate of lungs cancer among men in Africa

ii. *Women*

There were 20 data points from 14 African countries with a pooled incidence rate of 1.916/100,000 (1.347, 2.484). I^2 = 90.8%, p = 0.000 (**Figure 3.37**). In 2010, this would amount to about nine thousand new cases of lung cancer among women in Africa.

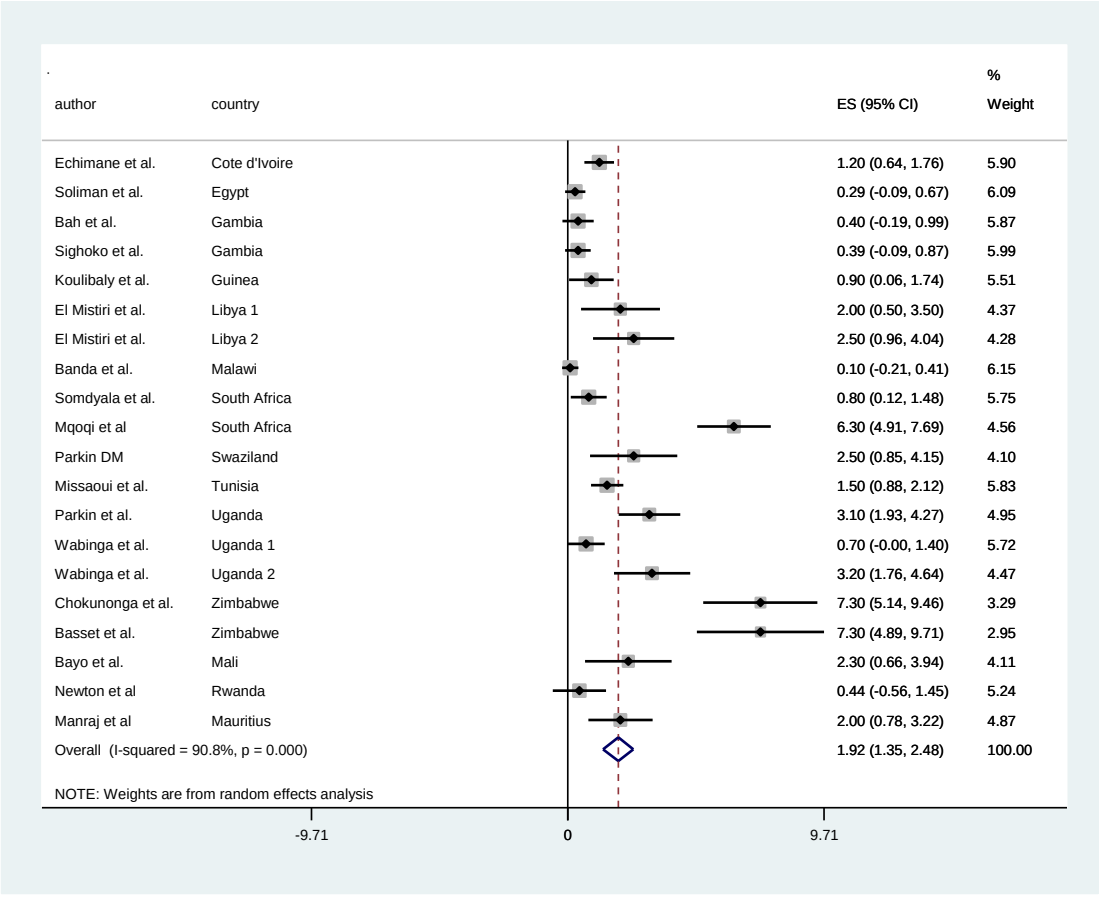

Figure 3.37. Forest plot showing pooled incidence rate of lungs cancer among women in Africa

3.4.10 Colorectal cancer

i. Men

There were 23 data points from 16 African countries with a pooled incidence rate of 5.257/100,000 (4.037, 6.476), I^2= 93.6%, p = 0.000 (**Figure 3.38**). In 2010, this would amount to over 27 thousand new cases of colorectal cancer among men in Africa.

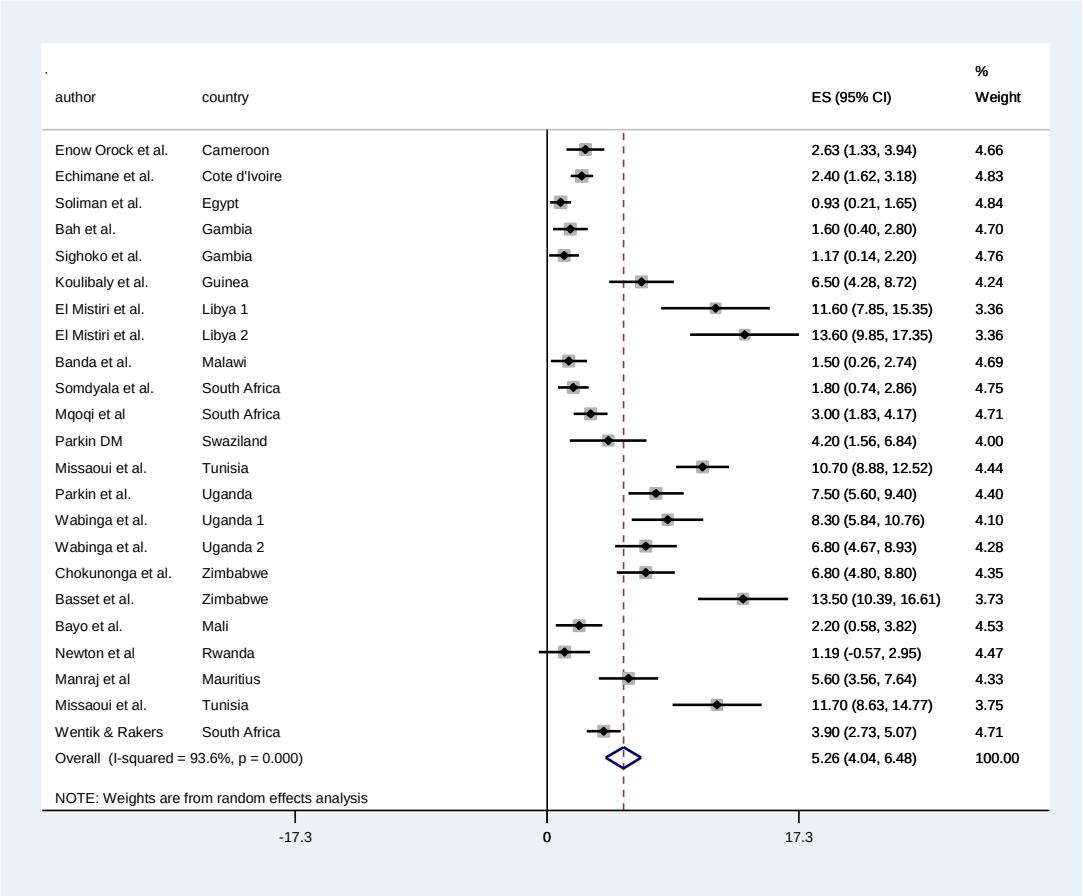

Figure 3.38. Forest plot showing pooled incidence rate of colorectal cancer among men in Africa

ii. Women

There were 23 data points from 16 African countries with a pooled incidence rate of 3.908/100,000 (2.939, 4.878), I^2 = 94.0%, p = 0.000 (**Figure 3.39**). In 2010, this would amount to about 18 thousand new cases of colorectal cancer among women in Africa.

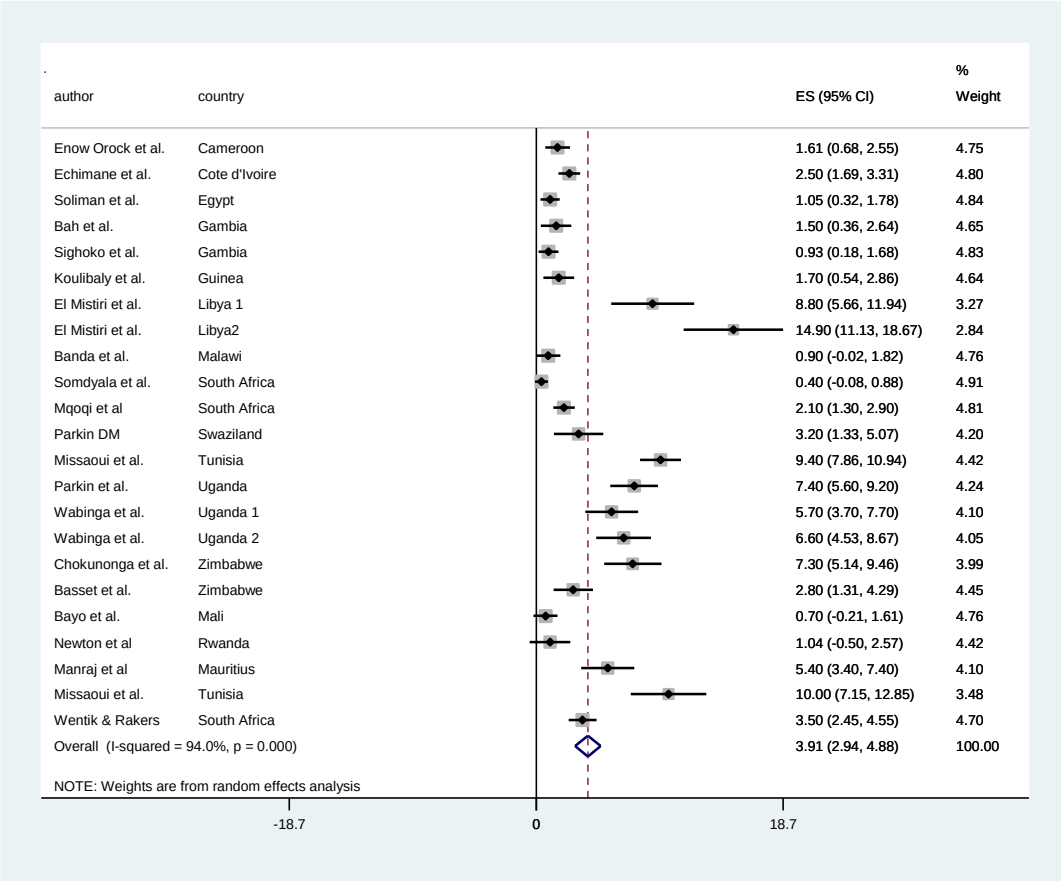

Figure 3.39. Forest plot showing pooled incidence rate of colorectal cancer among women in Africa

3.4.11 Stomach cancer

i. Men

There were 21 data points from 15 African countries with a pooled incidence rate of 5.627/100,000 (4.195, 7.060), I^2 = 95.0%, p = 0.000 (**Figure 3.40**). In 2010, this would amount to over 29 thousand new cases of stomach cancer among men in Africa.

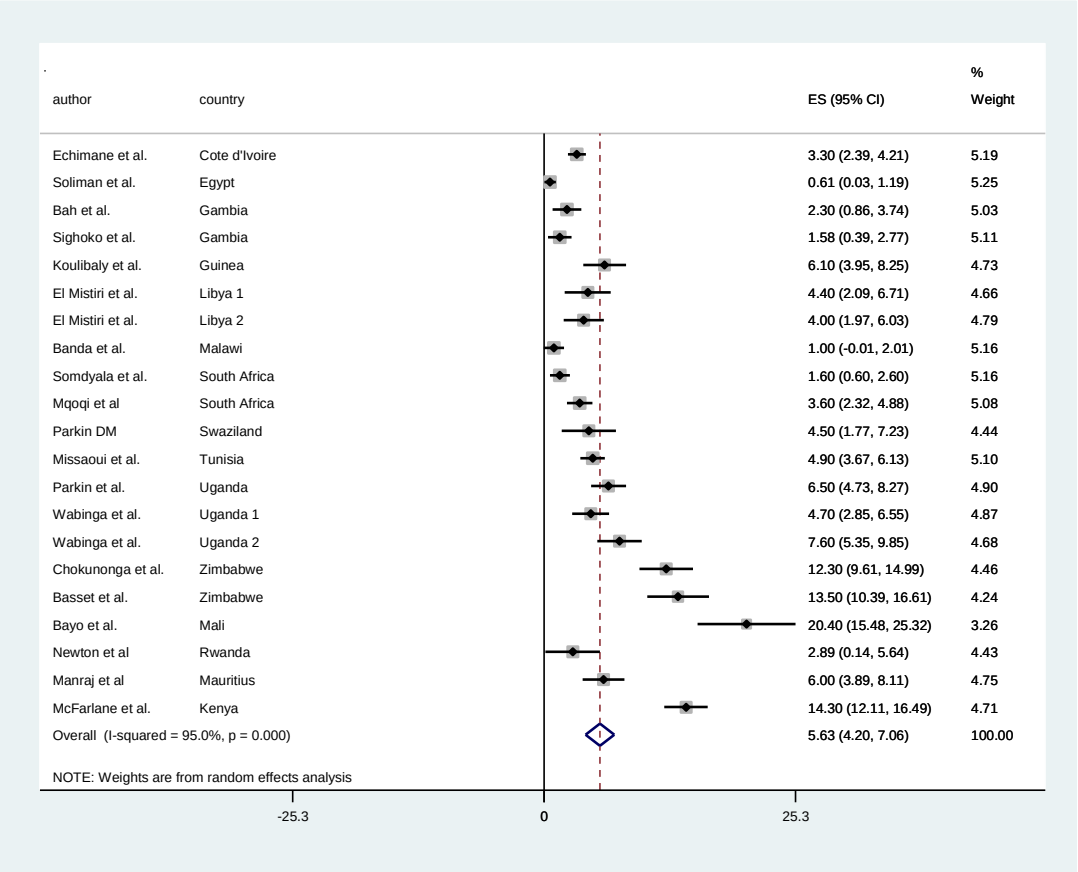

Figure 3.40. Forest plot showing pooled incidence rate of stomach cancer among men in Africa

ii. *Women*

There were 21 data points from 14 African countries with a pooled incidence rate of 3.8/100,000 (2.939, 4.661), I^2= 95.6%, p = 0.000 (**Figure 3.41**). In 2010, this would amount to over 17 thousand new cases of stomach cancer among women in Africa.

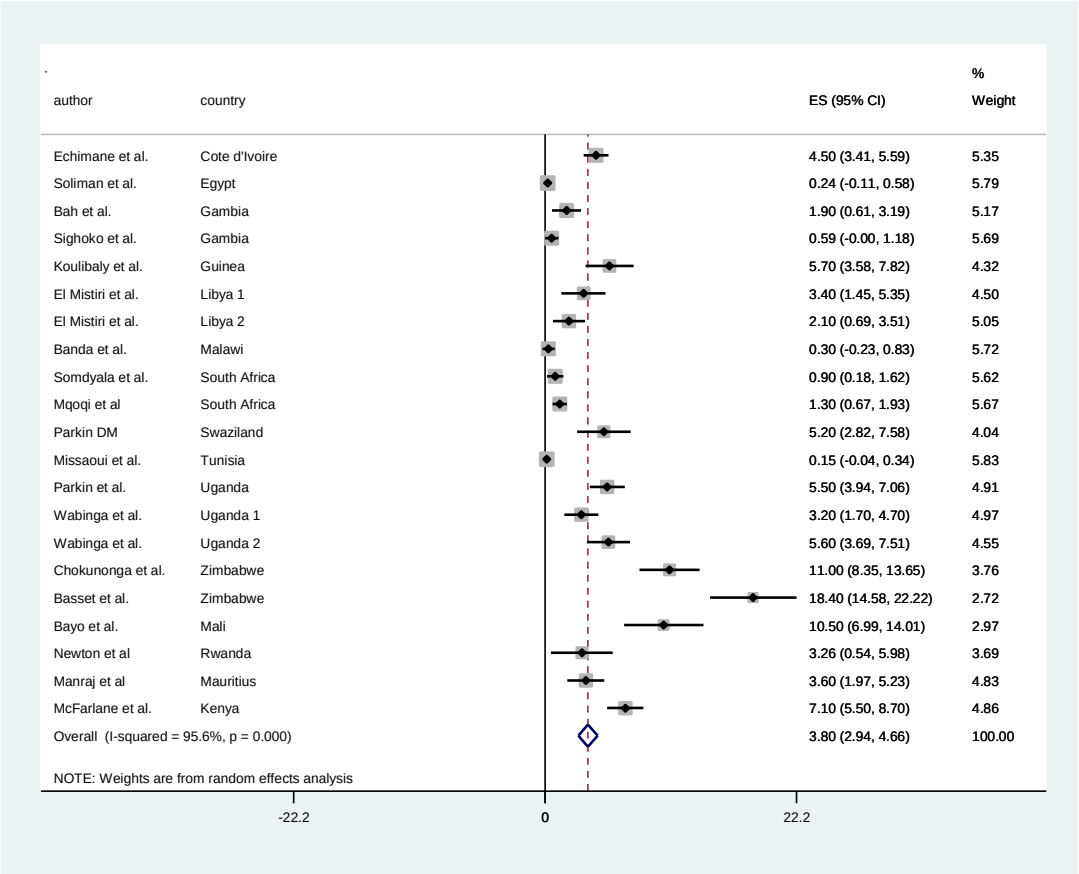

Figure 3.41. Forest plot showing pooled incidence rate of stomach cancer among women in Africa

3.4.12 Non-Hodgkin lymphoma

i. Men

There were 21 data points from 14 African countries with a pooled incidence rate of 3.906/100,000 (2.845, 4.967), I^2 = 94.1%, p = 0.000 (**Figure 3.42**). In 2010, this would amount to over 20 thousand new cases of non-Hodgkin's lymphoma among men in Africa.

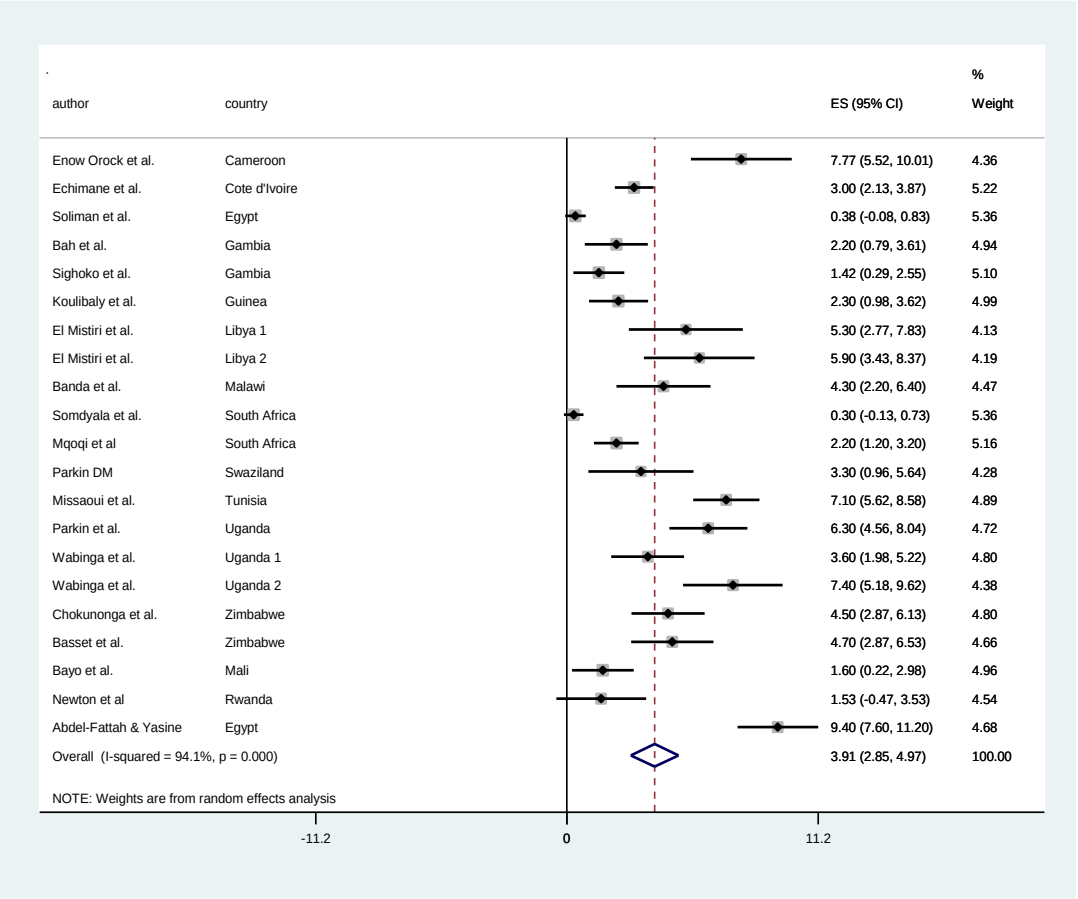

Figure 3.42. Forest plot showing pooled incidence rate of non-Hodgkin's lymphoma among men in Africa

ii. Women

There were 21 data points from 14 African countries with a pooled incidence rate of 2.865/100,000 (2.068, 3.663), I^2= 93.6%, p = 0.000 (**Figure 3.43**). In 2010, this would amount to over 13 thousand new cases of non-Hodgkin's lymphoma among women in Africa.

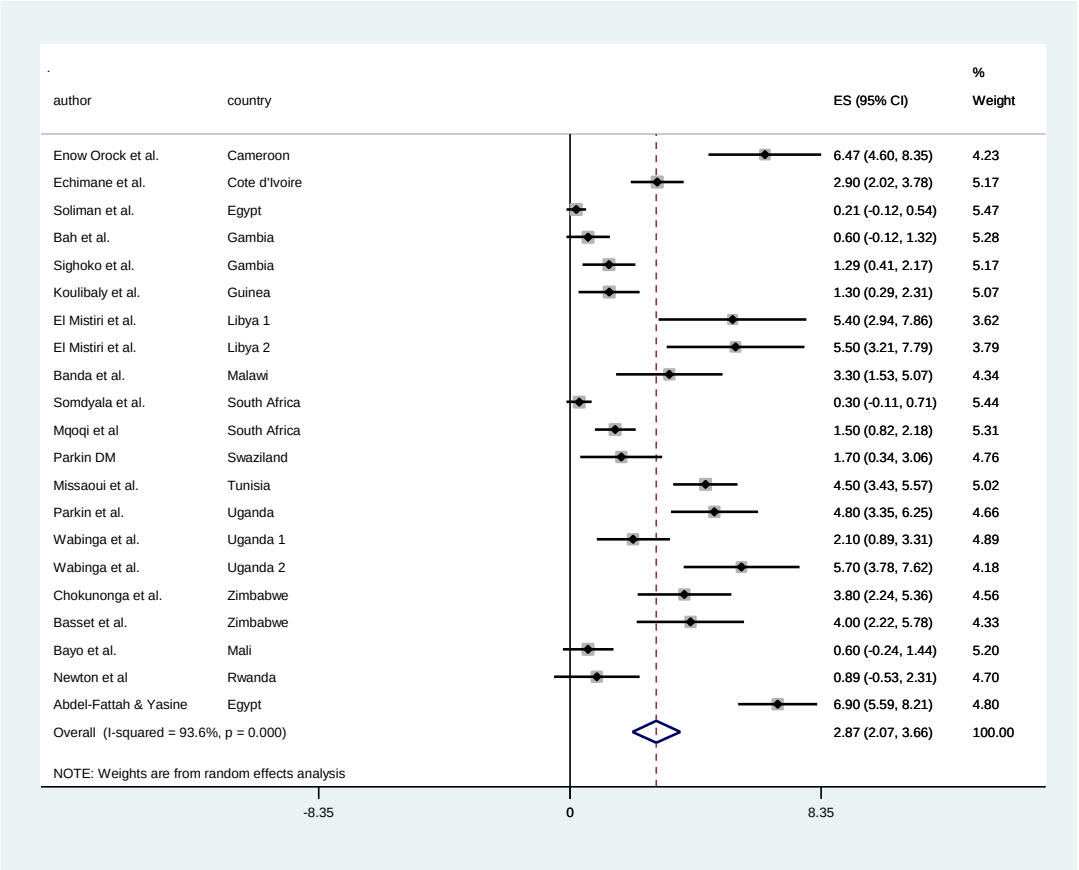

Figure 3.43. Forest plot showing pooled incidence rate of non-Hodgkin's lymphoma among women in Africa

3.5 CHRONIC RESPIRATORY DISEASES

3.5.1 Chronic Obstructive Pulmonary Disease (COPD)

Systematic review

The main literature search returned 243 studies, with Medline (66), EMBASE (144), and Global Health (33). 179 records remained after excluding duplicates. Two additional studies were included from the search of google scholar and the reference lists of relevant publications. On screening titles for relevance, 109 records were excluded, giving a total of 71 full-text articles assessed for eligibility. After applying the quality criteria, 58 studies were excluded; 33 articles did not provide prevalence of COPD or any relevant estimates from which prevalence can be calculated, and 25 articles did not specify study designs and / or clarify COPD case definitions. A total of 13 studies that met the overall selection criteria were finally retained for both qualitative synthesis and quantitative analysis (**Figure 3.44**).

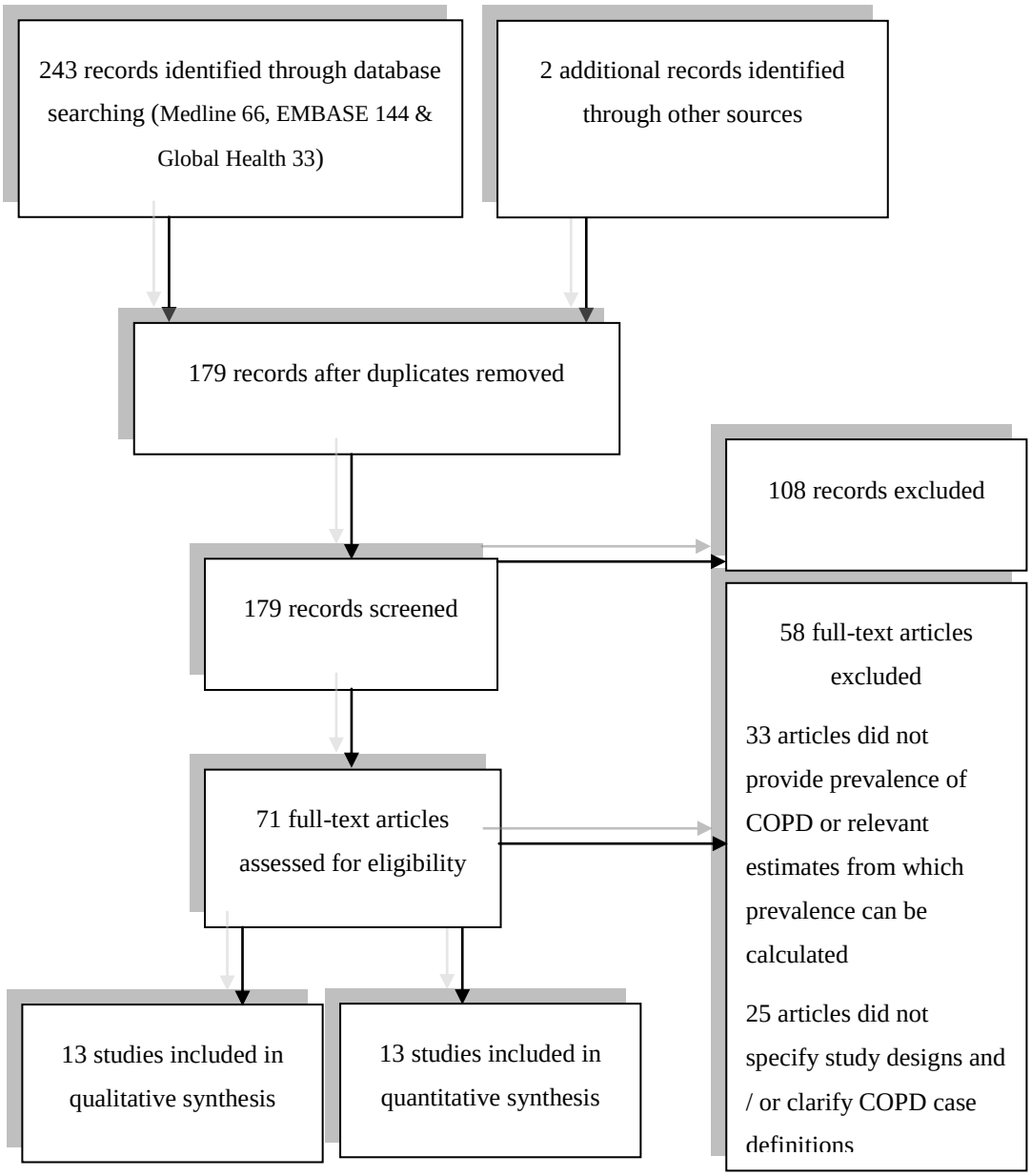

Figure 3.44. Flow diagram of search results for COPD in Africa

Study characteristics

The retained 13 studies were from 8 African countries, all spread across the main regions of Africa. South Africa and Nigeria had the highest number of studies retained, both with a total of 7 studies. Algeria, Ethiopia, Malawi, Morocco, Rwanda and Tunisia were the other countries from which retained studies were conducted, all with one study each (**Figure 3.45**).

Figure 3.45. Map of Africa with asterisks showing countries of the retained COPD studies.

On the type of study, there were 5 spirometric and 10 non-spirometric (other) studies, both study types with 13 and 20 data points, respectively. Two studies reported both spirometric and non-spirometric estimates (**Tables 3.28 and 3.29**).

Table 3.28. Characteristic distribution of retained COPD studies in Africa

Characteristics	***Country***	***Number of studies***
Central (1 study)	Rwanda	1
East (1 study)	Ethiopia	1
North (3 studies)	Algeria	1
	Morocco	1
	Tunisia	1
South (5 studies)	Malawi	1
	South Africa	4
West (3 studies)	Nigeria	3
Study type		
Spirometric		5
Nonspirometric		10
Reporting both		2
Study setting		
Rural		2
Urban		1
Mixed		6
Occupational		4
Study duration		
<1 year		7
1-3 years		5
>3 years		2
Sample size		
<1000		9
1001-3000		2
>3000		2

Table 3.29. Overall characteristics of retained COPD studies in Africa

African region	*Country, Location*	*Study setting*	*Study period*	*Age range/ Mean age*	*Case definition*
Central	1) Rwanda, Kigali (Musafiri et al., 2011b)	Mixed	2008 -2009	≥15 years (mean age 38.3 years)	ATS/ERS guidelines: FEV_1/FVC < LLN. LLN= lower limit of normal, which is 5th percentile (1.645 SD below predicted); BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
East	2) Ethiopia, Addis Ababa (Mengesha and Bekele, 1998)	Occupational	1997-1998	37±8.0 years	BMRC (1965) & ATS (1962) criteria: productive cough for >3 months/year for at least 2 successive years
North	3) Algeria, Algiers (Khelafi et al., 2011)	Mixed	2009	21-89 years	GOLD criteria: postbronchodilator FEV1/FVC < 0.7
	4) Morocco, Rabat (Laraqui Hossini et al., 2002)	Occupational	2001-2002	≥15 years	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
	5) Tunisia, Tunis (Tabka et al., 1999)	Occupational	1998	≥15 years	BMRC criteria: productive cough for >3 months/year for at least 2 successive years
South	6) Malawi, Blantyre and Chikwawa districts (Fullerton et al., 2011)	Mixed Urban and Rural	2001	≥30 years (mean age 45.0 years)	ATS/ERS criteria: FEV_1/FVC < 0.7
	7) South Africa, National DHS (Ayo-Yusuf et al., 2008)	Mixed	1998	≥25 years	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
	8) South Africa, Cape town (Buist et al., 2007)	Mixed	2004-2006	≥40 years	GOLD criteria: postbronchodilator FEV_1/FVC < 0.7

	9) South Africa, National Household Survey (Ehrlich et al., 2004)	Mixed	2004	≥15 years	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
	10) South Africa, Basotho (Girdler-Brown et al., 2008)	Occupational	2007-2008	Mean age 49.4 years	ATS/ERS criteria: $FEV_1/FVC < 0.7$; BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
West	11) Nigeria, Ekiti State (Desalu, 2011)	Rural	2009	≥35 years (mean age 55.5±10.2)	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
	12) Nigeria, Ijero-Ekiti (Desalu et al., 2010)	Rural	2009	55 ± 10 years	ECRHS & BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
	13) Nigeria, Benin (Gathuru et al., 2002)	Urban	1992-1999	30-69yrs (mean age 48.8 years)	ATS/ERS criteria: $FEV_1/FVC < 0.7$; BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years

ATS: American Thoracic Society, BMRC: British Medical Research Council, DHS: Demographic and Health Survey, ECRHS: European Community Respiratory Health Survey, ERS: European Respiratory Society, FEV1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity, GOLD: Global Initiative for chronic Obstructive Lung Disease, LLN: lower limit of normal

The mean ages of subjects from retained studies were 55.2 years and 49.2 years in spirometric and non-spirometric studies, respectively. For the verification of ages cross most studies, birth certificates were usually employed in determining the age of subjects, and in the absence of any valid birth certificates or age-verification documents, historical landmarks associated with the birth of the subject were employed in estimating the age.

Periods of study were mostly within one year (7 studies). The total sample size from all retained studies was 24,747. Across individual studies, the mean sample size from all studies was 1241 (median 416), and the study settings were mainly mixed (6 studies) (see **Tables 3.28 and 3.29**).

Details of quality criteria and grading of retained COPD studies in Africa

Of the retained 13 studies, four studies were graded as low quality (**Table 3.30**). These studies had well explained study designs, however, study population were not representative of a larger population group, these studies were based on purposive sampling and were mainly conducted within occupational settings, and thus they could be potential sources of heterogeneities if a pooled COPD prevalence was estimated.

Table 3.30. Quality assessment of retained COPD studies in Africa

Study ID*	***Study design***	***Study analysis***	***Study limitations***	***Generalizability to Africa***	***Grading***
1, 3, 8, 9, 11-13	Well explained across all studies	Well explained across all studies	Well-presented across all studies	Study population representative of a larger African population	*High*
7	Well explained	Not well explained	Not well-presented	Study population representative of a larger African population	*Moderate*
2, 4, 5, 10	Well explained	Not well explained	Not well presented	Study population not fairly representative of a larger African population	*Low*

see **Table 3.29 for details of Study ID*

Distribution of crude prevalence estimates of COPD in Africa

The COPD prevalence reported by spirometric studies was generally higher than the non-spirometric (other) studies. Across the spirometric study, the highest COPD prevalence was reported in South Africa in 2006 (prevalence 23.8%, mean age 53.5 years) (Buist et al., 2007), while the lowest COPD prevalence was reported in Algeria in 2009 (prevalence 9.2%, mean age 55 years) (Khelafi et al., 2011). Across non-spirometric (other) studies, the highest COPD prevalence was reported among cement factory workers in Morocco in 2002 (prevalence 25.2%, mean age 44.5 years) (Laraqui Hossini et al., 2002), while the lowest COPD prevalence was reported in Nigeria in 1999 (prevalence 1.7%, mean age 48.8 years) (Gathuru et al., 2002).

From the analysis and to allow for detailed comparisons, the estimates of COPD prevalence rates for the two types of data were reported separately for spirometry-based and non-spirometric (other) studies, respectively (**Table 3.31**; **Figure 3.46**). As noted in the methods, due to the significant heterogeneities among retained studies, a meta-analysis (pooled estimate) and modelling could not be conducted, a descriptive statistics is therefore reported (**Table 3.31)**. The mean prevalence of COPD from spirometry-based studies is 15.6% (standard deviation of 7.9%), while the median prevalence 13.4% (IQR: 9.4%-22.1%). From the non-spirometric (other) studies, the estimated mean prevalence of COPD is 7.0% (standard deviation of 7.2%), while the median prevalence is 4.0% (IQR: 2.1%-8.9%). This difference is statistically significant (p=0.001 for comparison of medians and p=0.003 for comparison of means). For other covariates, such as the year of study, mean age, the number of cases and sample sizes, the descriptive statistics are shown in **Table 3.31**.

When the estimates from spirometric studies was applied to the appropriate age group as observed from selected studies (40 years or more), which accounted for 196.4 million people in Africa in 2010, the estimated median prevalence (13.4%) translates into 26.3 million (18.5-43.4 million) cases of COPD. Comparable figures for the year 2000 based on the same prevalence rates would amount to 20.0 million

(14.1-33.1), suggesting an increase of 31.5% over a decade that is attributable mainly to ageing and growth of the African population.

Table 3.31. Descriptive statistics for year, mean age, number of cases, sample size and prevalence of COPD in Africa for the spirometry-based studies and non-spirometric (other) studies

Spirometry-based studies

Statistics		Year	Mean age	No. of cases	Sample size	% prevalence of COPD
Data points		13	13	13	13	13
Mean		2004.85	55.2462	55.57	389.85	15.5946
Median		2006.00	53.5000	45.00	290.00	13.4000
Std. Deviation		3.934	11.49461	50.329	285.518	7.91887
Range		10	39.50	191	896	24.15
Percentiles	25	2000.00	46.9000	20.11	160.00	9.3700
	75	2008.50	62.0000	77.84	633.00	22.0500

Other studies

Statistics		Year	Mean age	No. of cases	Sample size	% prevalence of COPD
Data points		20	20	20	20	20
Mean		2004.65	49.1750	68.52	1797.10	7.0015
Median		2004.00	49.1000	55.50	516.00	4.0350
Std. Deviation		4.043	14.29497	84.273	3044.636	7.18240
Range		11	60.00	358	13411	23.80
Percentiles	25	2002.50	39.5000	6.81	116.75	2.1225
	75	2009.00	58.5000	80.00	2260.50	8.8500

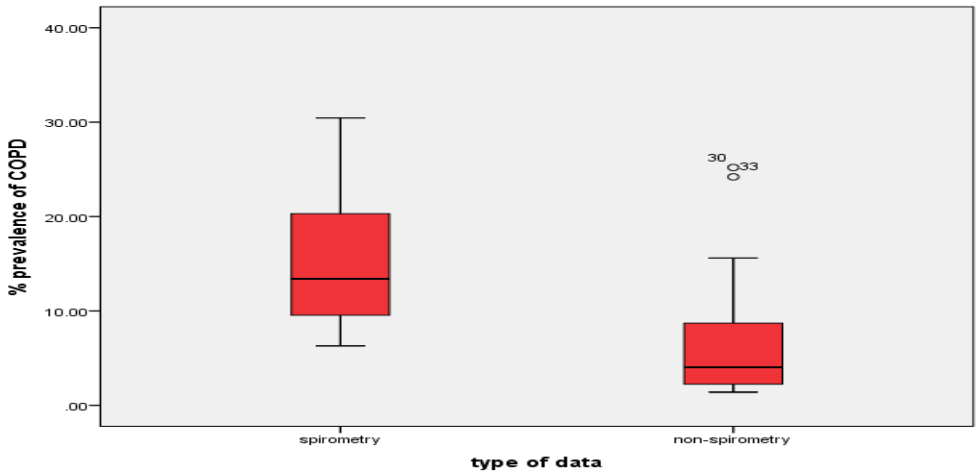

Figure 3.46. Boxplots of the prevalence of COPD in Africa for spirometric and non-spirometric (other) studies

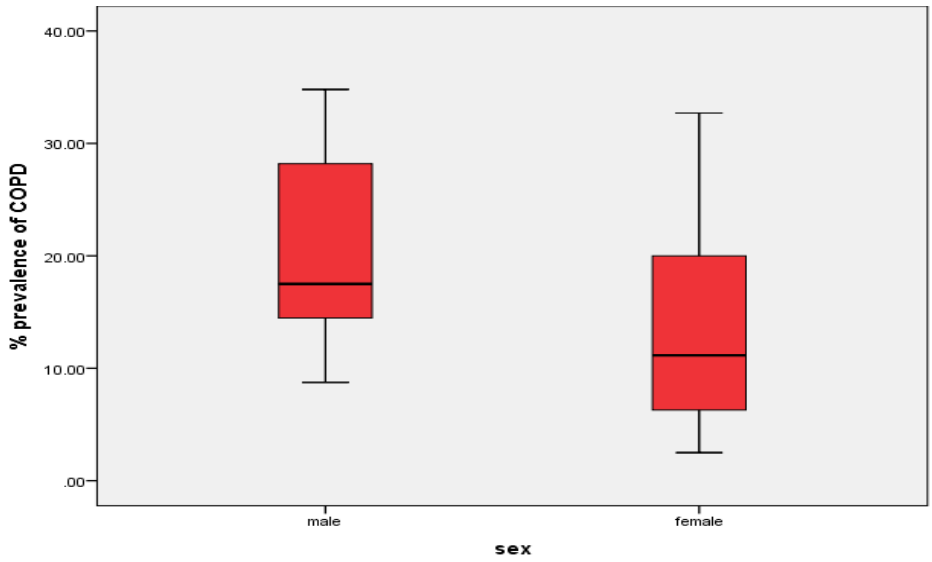

Figure 3.47. Boxplots of COPD prevalence in Africa by gender for spirometric studies

COPD prevalence estimates in Africa by gender

From studies based on spirometry, the mean COPD prevalence among men was 19.7% (standard deviation 8.4%), and the median prevalence was 17.5% (IQR: 2.7%-32.3%). While the mean COPD prevalence among women was 13.9% (standard deviation 9.8%), and the median prevalence was 11.2% (IQR: 2.5%-26.4%) (**Table 3.32** and **Figure 3.47**).

Table 3.32. Analysis of COPD prevalence in Africa by gender for spirometric studies

Sex	*Statistics*		*% prevalence of COPD*
male	Mean		19.7360
	95% Confidence Interval for Mean	Lower Bound	13.7212
		Upper Bound	25.7508
	Median		17.5000
	Std. Deviation		8.40805
	Minimum		8.75
	Maximum		34.80
	Range		26.05
	Interquartile Range		14.84
female	Mean		13.8650
	95% Confidence Interval for Mean	Lower Bound	6.8850
		Upper Bound	20.8450
	Median		11.1550
	Std. Deviation		9.75737
	Minimum		2.50
	Maximum		32.70
	Range		30.20
	Interquartile Range		15.17

Meanwhile, from studies based on other definitions (non-spirometirc), the mean COPD prevalence among men was 3.2% (standard deviation 1.8%), and the median prevalence was 2.4% (IQR: 0.9%-9.0%). While the mean COPD prevalence among women was 3.6% (standard deviation 2.0%), and the median prevalence was 3.3% (IQR: 1.1%-6.8%) (**Table 3.33** and **Figure 3.48**).

Table 3.33. Analysis of COPD prevalence in Africa by gender for non-spirometric studies

Sex	*Statistics*		*% prevalence of COPD*
male	Mean		3.2178
	95% Confidence Interval for Mean	Lower Bound	1.8307
		Upper Bound	4.6049
	Median		2.4000
	Std. Deviation		1.80453
	Minimum		.90
	Maximum		6.70
	Range		5.80
	Interquartile Range		2.57
female	Mean		3.5640
	95% Confidence Interval for Mean	Lower Bound	2.1220
		Upper Bound	5.0060
	Median		3.2500
	Std. Deviation		2.01573
	Minimum		1.14
	Maximum		7.40
	Range		6.26
	Interquartile Range		3.45

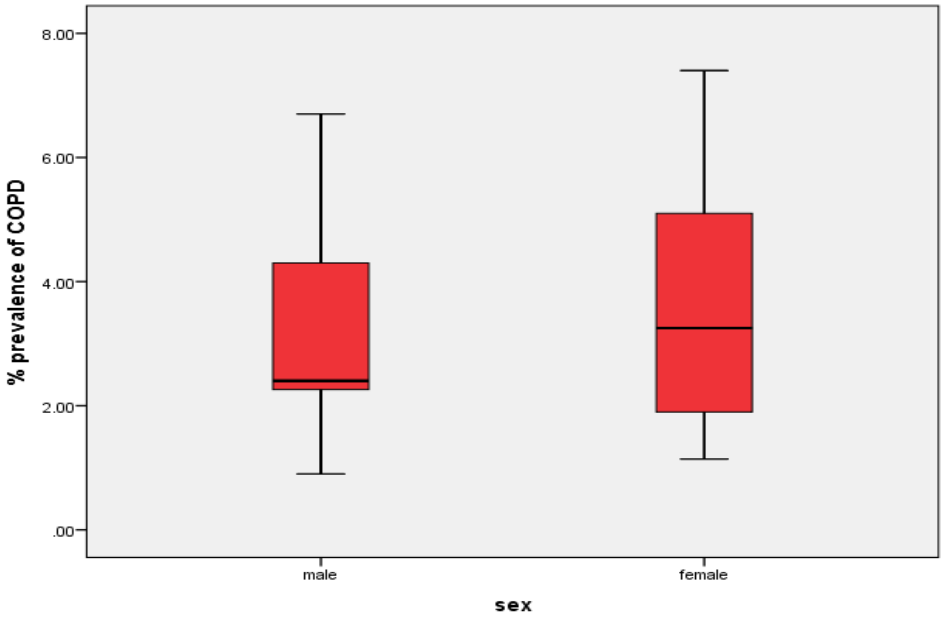

Figure 3.48. Boxplots of COPD prevalence in Africa by gender for non-spirometric studies

Further comparisons of spirometric and non-spirometric data

A further analysis of COPD prevalence and the estimated mean age revealed a significant positive correlation between the prevalence of COPD and the mean age in the spirometry-based set of studies (see **Table 3.34** and **Figure 3.49**), with the Pearson correlation coefficient of 0.645 (p-value = 0.017). This is a plausible finding as observed from many epidemiological surveys, and further suggests internal consistency of spirometry-based estimates.

Table 3.34. Pearson correlation coefficient between prevalence of COPD and mean age (spirometric studies)

		Mean age	*% prevalence of COPD*
% prevalence of COPD	Pearson Correlation	.645*	1
	Sig. (2-tailed)	.017	
	N	13	13

**. Correlation is significant at the 0.05 level (2-tailed). r = 0.645, p = 0.017 -> significant positive correlation*

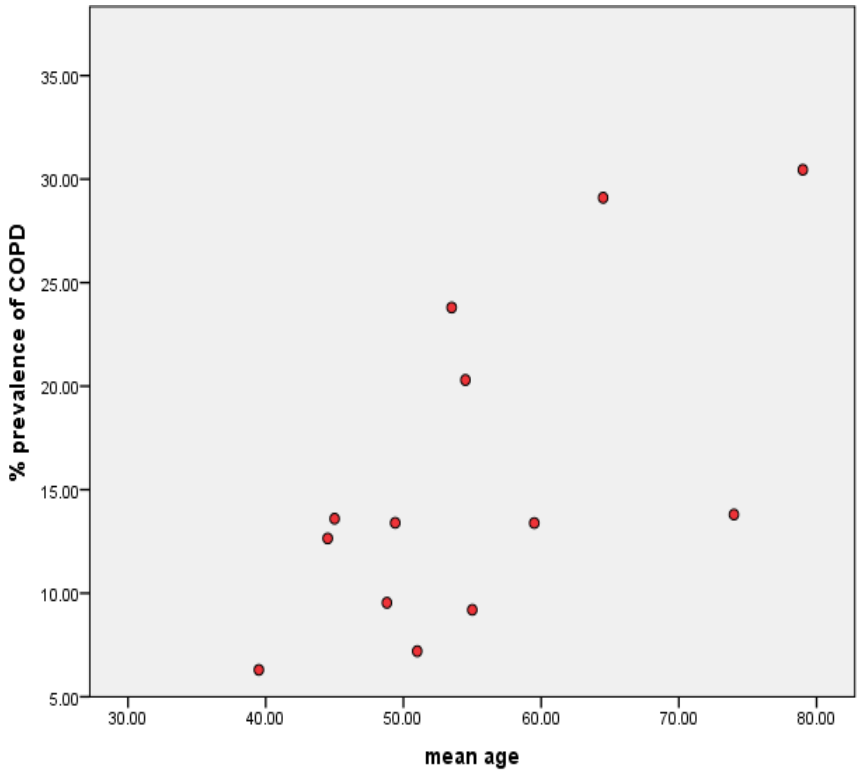

Figure 3.49. Plot of the prevalence of COPD in Africa versus the mean age from the spirometry-based studies.

There was no significant correlation between prevalence and age in non-spirometric (other) studies, with Pearson correlation coefficient of -0.011 (p>0.05) (see **Table 3.35** and **Figure 3.50**).

Table 3.35. Pearson correlation coefficient between prevalence of COPD and mean age (non-spirometric studies)

		Mean age	*% prevalence of COPD*
% prevalence of COPD	Pearson Correlation	-.011	1
	Sig. (2-tailed)	.964	
	N	20	20

p > 0.05: no significant correlation with age

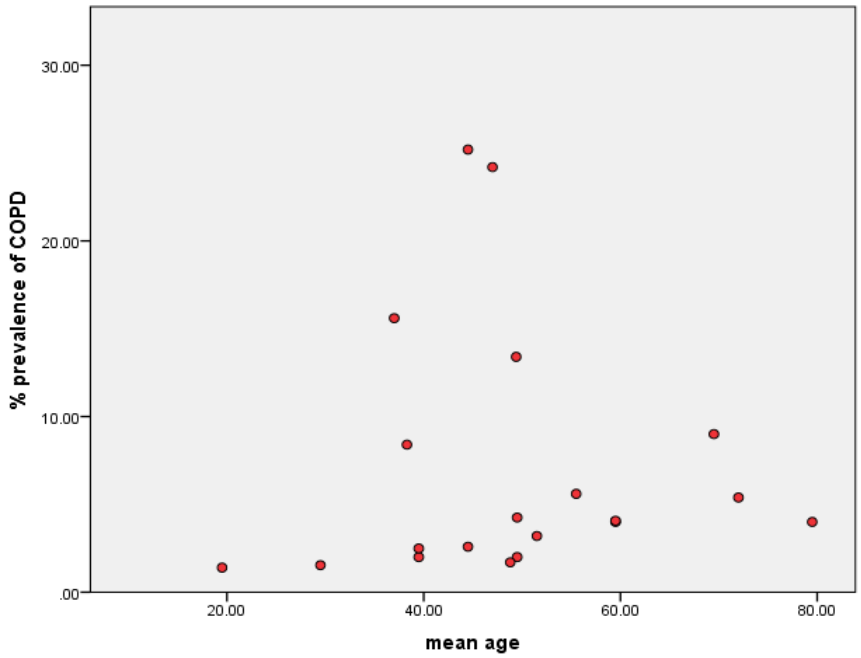

Figure 3.50. Plot of prevalence of COPD versus mean age from non-spirometric studies

3.5.2 Asthma

Systematic review

The main search initially returned 790 studies, with Medline yielding 246, EMBASE 370, and Global Health 174. Three additional records were identified from other sources (Google Scholar and reference lists of relevant publications). 522 studies remained after duplicates were removed. After screening the titles for relevance (i.e. asthma studies conducted primarily in an African population setting), 375 studies were excluded, giving a total of 147 full-texts articles that were assessed. On applying the quality criteria, 102 full-text articles excluded (54 articles did not provide prevalence of asthma or wheeze or related asthma symptoms or relevant estimates from which prevalence can be calculated , and 48 articles did not specify study designs and / or clarify asthma symptoms used for diagnosis). A total of 45 studies were finally retained for the review (**Figure 3.51**). The relatively higher number of retained studies (compared to initial output of 790) was because many of these studies were broadly based on all or any of the respiratory symptoms of asthma as described by GINA, which included: wheeze at rest, wheeze on exercise, nocturnal wheeze, nocturnal cough, or severe wheeze.

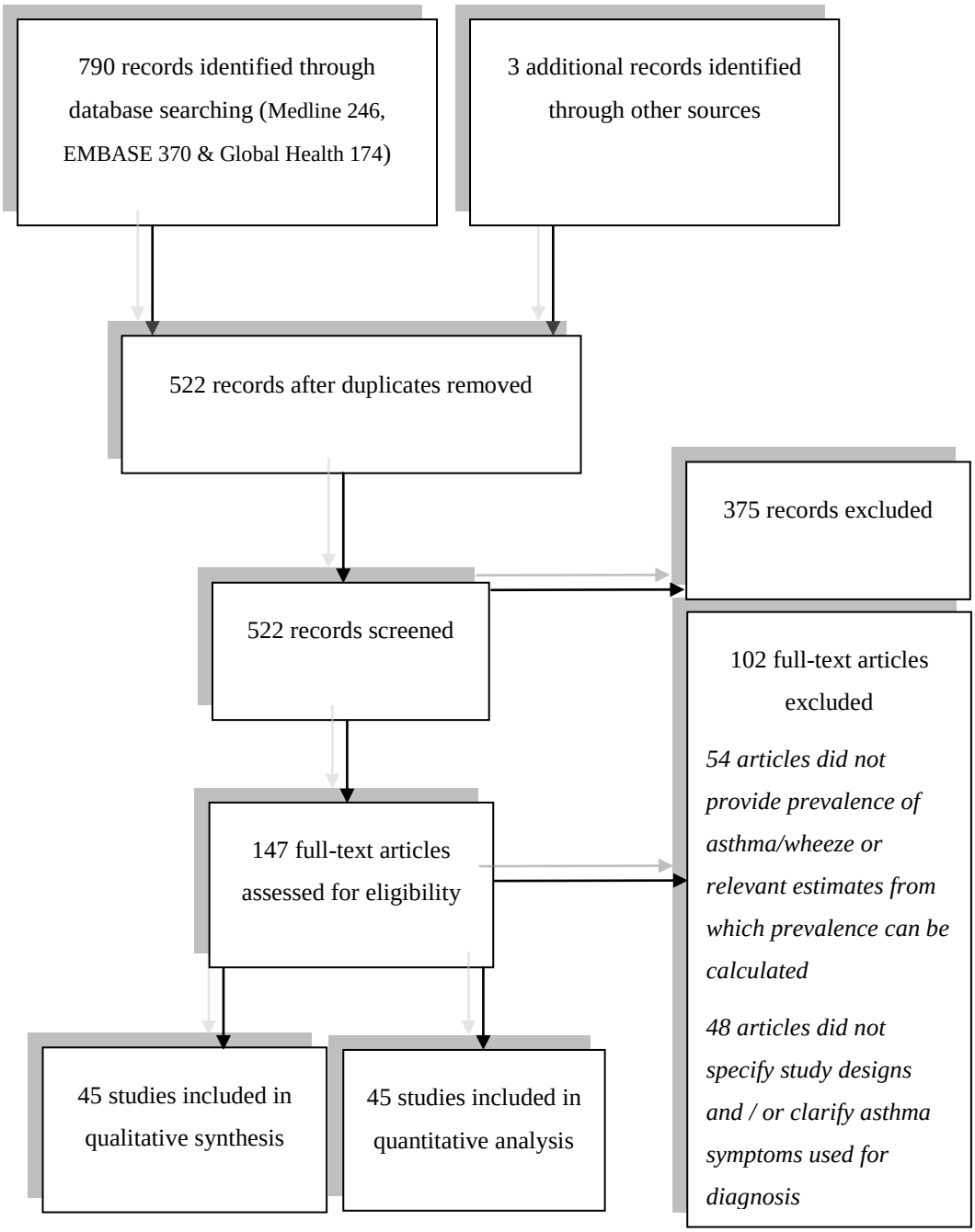

Figure 3.51. Flow diagram of search results for asthma in Africa

Study characteristics

The 45 retained studies were from 24 African countries spread across the main African regions. South Africa (11 study sites) and Nigeria (8 study sites) had the highest publication outputs. Ethiopia and Kenya closely followed with 6 and 5 study sites respectively, while Algeria, Morocco and Tunisia in North Africa had 4 study sites each (**Figure 3.52**). In all, there were a total of 64 study sites, with the ISAAC study I and III (Ait-Khaled et al., 2007b, Zar et al., 2007), providing about 50% of the data points employed in the final analysis

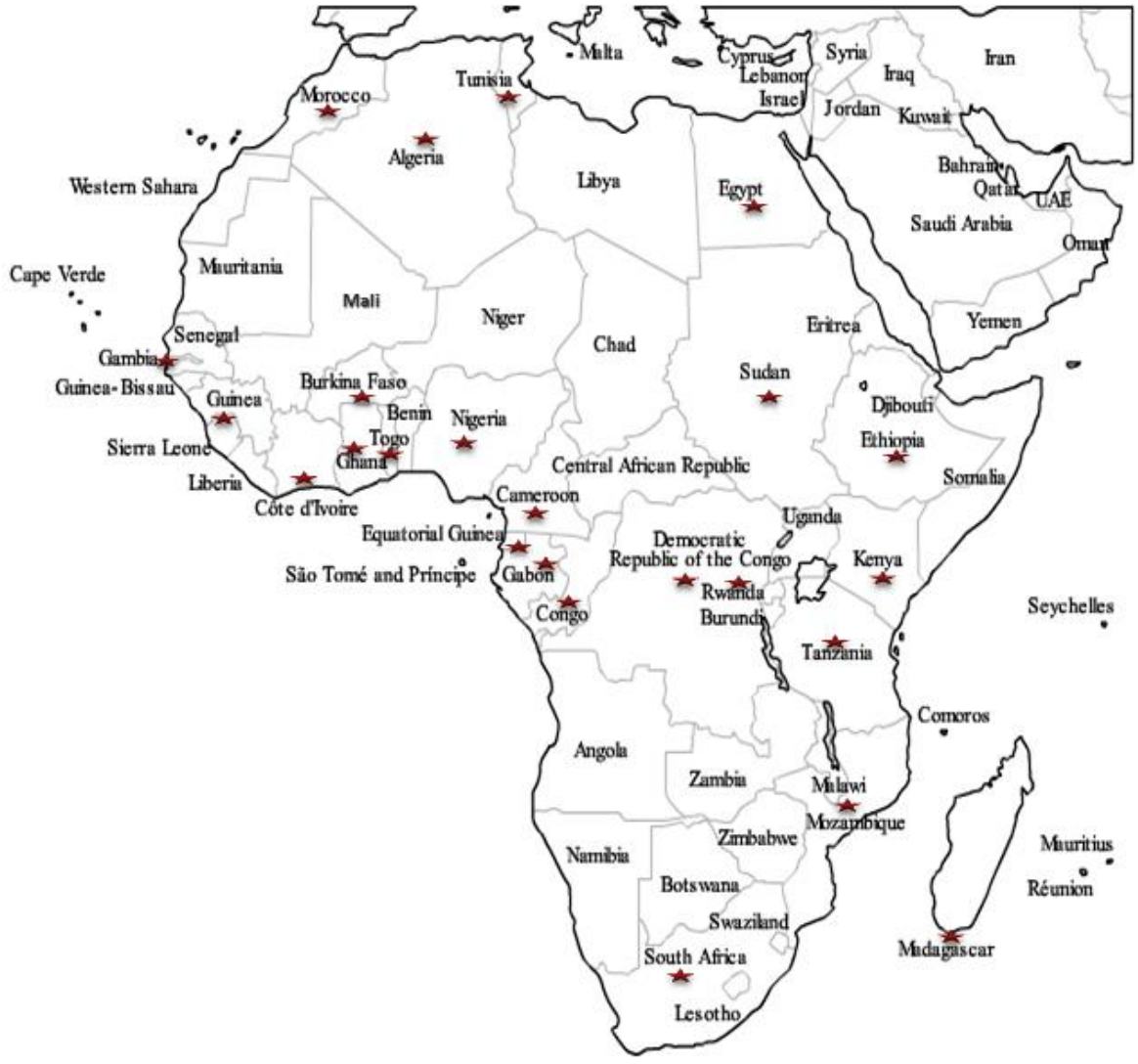

Figure 3.52. Map of Africa with asterisks showing countries of the retained asthma studies

14 studies were conducted in collaboration with the ISAAC group (31 studies did not have any collaboration). However, on the overall, 39 studies followed the general guidelines for the conduct of epidemiological surveys on asthma proposed by the ISAAC group, which involved both written and video questionnaires, respectively.

Many studies were conducted within one year (23 studies). The total sample size from all retained studies was 187,904. Across individual studies, sample sizes were mostly less than 1000 (mean 3243; median 2067). The study settings were predominantly mixed (urban and rural) (36 studies) (**Tables 3.36** and **3.37**).

Many studies were conducted mainly on paediatric subjects, mostly defined as less than 15 years of age, with a mean and median age of 13.7 years and 13.5 years, respectively. For the age determination of subjects from most studies, birth certificates were usually employed.

Table 3.36. Distribution of retained asthma studies in Africa

Characteristics	***Country***	***Study sites***
Central (6 study sites)	Cameroon	1
	Cape Verde	1
	Congo Brazzaville	1
	DR Congo	2
	Rwanda	1
East (14 study sites)	Ethiopia	6
	Kenya	5
	Sudan	2
	Tanzania	1
North (13 study sites)	Algeria	4
	Egypt	1
	Morocco	4
	Tunisia	4
South (13 study sites)	Madagascar	1

	Mozambique	1
	South Africa	11
West (18 study sites)	Burkina Faso	2
	Cote d'Ivoire	3
	Gabon	1
	Gambia	1
	Ghana	1
	Guinea	1
	Nigeria	8
	Togo	1
Duration of study		
<1 year		23
1-3 years		16
>3 years		6
Sample size		
<1000		18
1001-3000		15
>3000		12
Study setting		
Rural		3
Urban		6
Mixed		30
Occupational		8
Study type		
ISAAC guidelines		14
Non-ISAAC guidelines		31
Written questionnaire		39
Video questionnaire		6

Table 3.37. Overall characteristics of retained asthma studies

African region	*Country*	*Study Period*	*Study Setting*	*Age range/ Mean age*	*Diagnosis*
Central	1) ISAAC III study (selected countries in Africa) (Ait-Khaled et al., 2007b)	2000-2003	Mixed	6-7 years; 13-14 years	ISAAC guidelines and scores: based on asthma symptoms (wheeze at rest, wheeze after/during exercise, nocturnal wheeze, nocturnal cough, severe wheeze with speech limitation) using written or video questionnaires
	2) ISAAC I study (selected countries in Africa) (Zar et al., 2007)	1994-1995	Mixed	6-7 years; 13-14 years	ISAAC guidelines and scores: based on asthma symptoms (wheeze at rest, wheeze after/during exercise, nocturnal wheeze, nocturnal cough, severe wheeze with speech limitation) using written or video questionnaires
	3) Cape Verde (Morais de Almeida et al., 2001)	1993	Mixed	6-10 years	GINA criteria; "Asthma ever was defined as the cumulative lifetime diagnosis. Active asthma identified in children with symptoms during the previous year, and current asthma was considered if a positive bronchial challenge test was found in children with active asthma"
	4) DR Congo (Nyembue et al., 2012)	2010	Mixed	29±16 years	GINA criteria; Asthma symptoms, physician's diagnosis, skin prick test, written questionnaire

	5) Rwanda (Musafiri et al., 2011b)	2008-2009	Mixed	≥15 years	ATS criteria; Asthma symptoms, physician's diagnosis, written questionnaire; Subjects who presented with reversible airways obstruction (pre-bronchodilator FEV1/FVC < LLN and a positive reversibility test meaning an increase in FEV1 of 200 ml and 12% with respect to pre-bronchodilator FEV1 after 400 mcg of salbutamol)
East	6) Ethiopia (Dagoye et al., 2003)	2003	Mixed	1-5 years	ISAAC guidelines, physician's diagnosis, written questionnaire
	7) Ethiopia (Hailu et al., 2003)	1997	Mixed	13-14 years	ISAAC guidelines, written questionnaire
	8) Ethiopia (Mengesha and Bekele, 1998)	1997	Occupational	>20 years	Asthma symptoms, physician's diagnosis, written questionnaire
	9) Ethiopia (Yemaneberhan et al., 1997)	1996	Mixed (Urban/Rural)	22.8 years	IUATLD (1984) questionnaire
	10) Kenya (Esamai and Anabwani, 1996)	1995	Rural	13-14 years	ISAAC guidelines, written/video questionnaire
	11) Kenya (Esamai et al., 2002)	2001	Rural	13-14 years	ISAAC guidelines, written/video questionnaire
	12) Kenya (Ng'ang'a et al., 1998)	1996	Mixed	10.6 years	6 min free running test (6MFRT), drop in post exercise PEFR ≥15% or >=10% classified as EIB

	13) Kenya (Odhiambo et al., 1998)	1993	Mixed (Urban/Rural)	10.8 years	IUATLD (1984) guidelines; Asthma symptoms, physician's diagnosis, written questionnaire
	14) Tanzania (Berntsen et al., 2009)	2008	Mixed	9-10 years	ISAAC guidelines and scores: based on asthma symptoms (wheeze at rest, wheeze after/during exercise, nocturnal wheeze, nocturnal cough, severe wheeze with speech limitation) using mainly video questionnaires
North	15) North Africa-Algeria, Morocco & Tunisia (AIRMAG study) (Nafti et al., 2009)	2008	Mixed	13-14 years; >25 years	GINA criteria "Have you had an asthma attack or asthma symptoms in the previous twelve months? Have you taken medication for asthma attacks (eg pills, inhaled powders, aerosols etc) in the previous twelve months? Have you taken ventolin in the previous twelve months?"
	16) Algeria (Bezzaoucha, 1992)	1991	Mixed	<25 years	Asthma symptoms, physician's diagnosis, written questionnaire
	17) Algeria (Benarab-Boucherit et al., 2011)	2010	Mixed	10-12 years	6 min free running test (6MFRT), drop in post exercise PEFR >=15% classified as EIB
	18) Egypt (Georgy et al., 2006)	2005	Mixed	11-15 years	ISAAC guidelines, written questionnaire

	19) Morocco (Bennis et al., 1992)	1991	Rural	< 15 years	Questionnaires based on: "Have you ever had whistling noises in the chest?", "Have you ever had a sensation of respiratory difficulty or suffocation with a whistling noise in the chest?", "Have you ever had asthma?"
	20) Morocco (Laraqui Hossini et al., 2002)	2001	Occupational	>20 years	ISAAC guidelines, written questionnaire
	21) Tunisia (Khaldi et al., 2005)	2004	Mixed	13-14 years	ISAAC guidelines, written questionnaire
	22) Tunisia (Sallaoui et al., 2007)	2003	Mixed	20.8±2.7 years	EIB classified as decrease of at least 15% in forced expiratory volume in one second (FEV1) after 8-min running at 80–85%
South	23) Madagascar (Wolff et al., 2012)	2010	Urban	7-14 years	Modified ISAAC questionnaire; bronchodilator response (BDR) to establish reversible obstruction (change in FEV1 ≥ 12%)
	24) Mozambique (Mavale-Manuel et al., 2006)	2005	Mixed	13-14 years	ISAAC guidelines, video questionnaire
	25) South Africa (Ehrlich et al., 1995)	1994	Mixed	<18 years	Asthma symptoms, physician's diagnosis, written questionnaire
	26) South Africa (Ehrlich et al., 1998)	1997	Mixed	5-12 years	Asthma symptoms, physician's diagnosis, written questionnaire (filled by parents)

	27) South Africa (Ehrlich et al., 2005)	2004	Mixed	>18 years	ECRHS guidelines, physician's diagnosis, written questionnaire
	28) South Africa (Mashalane et al., 2006)	2005	Mixed	9-10 years	Free Running Asthma Screening Test (FRAST); drop in post exercise PEFR ≥15% classified as EIB
	29) South Africa (Mtshali and Mokwena, 2009)	2007-2008	Mixed	8-16 years	Free Running Asthma Screening Test (FRAST drop in post exercise PEFR ≥10% on more than 2 occasions classified as EIB
	30) South Africa (Terblanche and Stewart, 1990)	1990	Mixed	5-15 years	6MFRT, 10% decline in forced expiratory volume in 1 second after exercise classified as EIB
	31) South Africa (Wichmann et al., 2009)	2004-2005	Urban	13-14 years	ISAAC guidelines, asthma symptoms, physician's diagnosis, written questionnaire
	32) South Africa (Nriagu et al., 1999)	1997-98	Urban	>15 years	Asthma symptoms using standard questionnaire recommended by the World Health Organization for asthma studies
	33) South Africa (Poyser et al., 2002)	2000	Mixed	13-14 years	ISAAC guidelines, written/video questionnaire
West	34) Burkina Faso (Miningou et al., 2002)	1998	Urban	15-64 years	Asthma symptoms, physician's diagnosis, written questionnaire
	35) Burkina Faso **(**Miszkurka et al., 2012)	2001	Mixed	>20 years	World Health Survey; Asthma symptoms, physician's diagnosis, written questionnaire
	36) Cote d'Ivoire (Koffi et al., 2000)	1998	Urban	13-14 years	ISAAC guidelines, written questionnaire

	37) Cote d'Ivoire (Roudaut et al., 1992)	1990	Mixed	10-17 years	Asthma symptoms, physician's diagnosis, written questionnaire
	38) Gambia (Walraven et al., 2001)	1996-1997	Mixed (Urban/Rural)	>15 years	IUATLD questionnaire; "Asthma defined by a medical history revealing the periodic occurrence of wheezing and/or (morning) dyspnoea and/or coughing in combination with a decrease of >20% in the FEV1 after provocation with methacholine inhalation at a range of concentrations up to 16 mg/mL, or a 15% increase in FEV1 from baseline 15 min after administering 400 mg inhaled salbutamol. Wheeze was defined as periodic whistling or tightness in the chest. 'Current wheeze' referred to wheezing in the previous 12 months"
	39) Ghana (Addo-Yobo et al., 2007)	1993; 2003	Mixed	9-16 years	6 min free running test (6MFRT), drop in post exercise PEFR ≥12.5% classified as EIB
	40) Nigeria (Falade et al., 2004)	1995	Mixed	13-14 years	ISAAC guidelines, written questionnaire
	41) Nigeria (Faniran et al., 1999)	1998	Urban	8-11 years	ISAAC guidelines, written questionnaire (modified from Institute of Respiratory Medicine, University of Sydney)

	42) Nigeria (Aguwa et al., 2007)	2006	Occupational	>20years	Asthma symptoms, physician's diagnosis, written questionnaire & spirometry (PEFR)
	43) Nigeria (Desalu et al., 2009)	2005-2006	Mixed	32+-10.12 years	ECRHS asthma-screening questionnaire, Subjects with FEV1 <80% of predicted, FEV1/FVC < 80%, or one asthma symptom were subjected to PEF variability testing
	44) Nigeria (Erhabor et al., 2006)	2005	Mixed	15-35 years	IUATLD (1984) & BMRC (1965) criteria
	45) Nigeria (Mustapha et al., 2011)	2004	Mixed	7-14 years	Asthma symptoms, physician's diagnosis, written questionnaire

6MFRT: 6 minute free running test, ATS: American Thoracic Society, BMRC: British Medical Research Council, EIB: exercise induced bronchospasm, ECRHS: European Community Respiratory Health Survey, FEV1: forced expiratory volume in one second, FRAST: free running asthma screening test, FVC: forced vital capacity, GINA: Global Initiative for Asthma, ISAAC: The International Study of Asthma and Allergies in Childhood, IUATLD: International Union Against Tuberculosis and Lung Diseases, LLN: lower limit of normal, PEFR: peak expiratory flow rate

Details of quality criteria and grading of retained asthma studies in Africa

Based on the quality grading criteria, most studies retained were graded as high quality. Due to the variations in diagnostic criteria for asthma, many studies adhered to the ISAAC guidelines for epidemiological surveys of asthma, and this allowed for some consistencies across all studies (**Table 3.38**)

Table 3.38. Quality assessment of retained asthma studies in Africa

*Study ID**	*Study design*	*Study analysis*	*Study limitations*	*Generalizability to Africa*	*Grading*
All studies except 8, 20 and 42	Well explained across all studies	Well explained across all studies	Well-presented across all studies	Study population representative of a larger African population	*High*
8, 20 and 42	Well explained	Not well explained	Not well presented	Study population not fairly representative of a larger African population	*Medium*

see **Table 3.37 for details of Study ID*

Distribution of crude prevalence of asthma in Africa from retained studies

Across retained studies, the prevalence rates of asthma in some parts of Africa were comparable with those reported from surveys in high-income settings. From studies based on written questionnaires, "asthma ever" (cumulative prevalence of asthma) was highest in South Africa (53%, 5-12 years) in 1997 (Ehrlich et al., 1998), followed by Egypt (26.5%, 11-15 years) in 2005 (Georgy et al., 2006), Nigeria (18.4%, 15-35 years) in 1995 (Erhabor et al., 2006), and Ethiopia (16.3%, >20 years) in 1997 (Mengesha and Bekele, 1998). The lowest prevalence was recorded in Gambia (1.9%, >15 years) in 1997 (Walraven et al., 2001). "Current wheeze" (wheeze at rest-12 month) was consistently high in South Africa, 26.8% (13-14 years) in 1994, 23.9% (5-12 years) in 1998, and 20.3% (13-14 years) in 2003

(Ehrlich et al., 1998, Ait-Khaled et al., 2007b, Poyser et al., 2002). From studies based on video questionnaires, "current wheeze" was highest in Morocco (12.9%, 6-7 years) in 2003 (Ait-Khaled et al., 2007b), and Tanzania (12.3%, 9-10 years) in 2008 (Berntsen et al., 2009), with South Africa recording the lowest prevalence (6.5%, 6-7 years) in 1995 and 2000 respectively (Poyser et al., 2002, Ait-Khaled et al., 2007b); there was no reported prevalence of "asthma ever" from studies based on video questionnaires (see **Tables 3.36** and **3.37**).

Pooled prevalence estimates of asthma in Africa

For the random effect meta-analysis, asthma diagnostic criteria based on "current wheeze" (wheeze at rest within 12 months) and "asthma ever" (cumulative prevalence of asthma) were employed, as these two criteria provided near clinical case diagnosis of asthma (Bousquet et al., 2010, IUATLD, 2011). In addition, data sets from written questionnaires were mainly used, due to the very limited data sets from video questionnaires, which could have allowed for more detailed comparisons. From all studies, the pooled crude prevalence for "current wheeze" was 13.5% (95% CI: 11.7-15.4, I=99.2%, p=0.000), with a mean age of 15.8 years. The pooled crude prevalence "asthma ever" was 9.5% (95% CI: 8.1-11.0, I=99.4%, p=0.000), mean age 19.6 years. The higher prevalence estimate from current wheeze may be indicative of the reported higher sensitivities from many asthma epidemiological surveys (**Figures 3.53** and **3.54**).

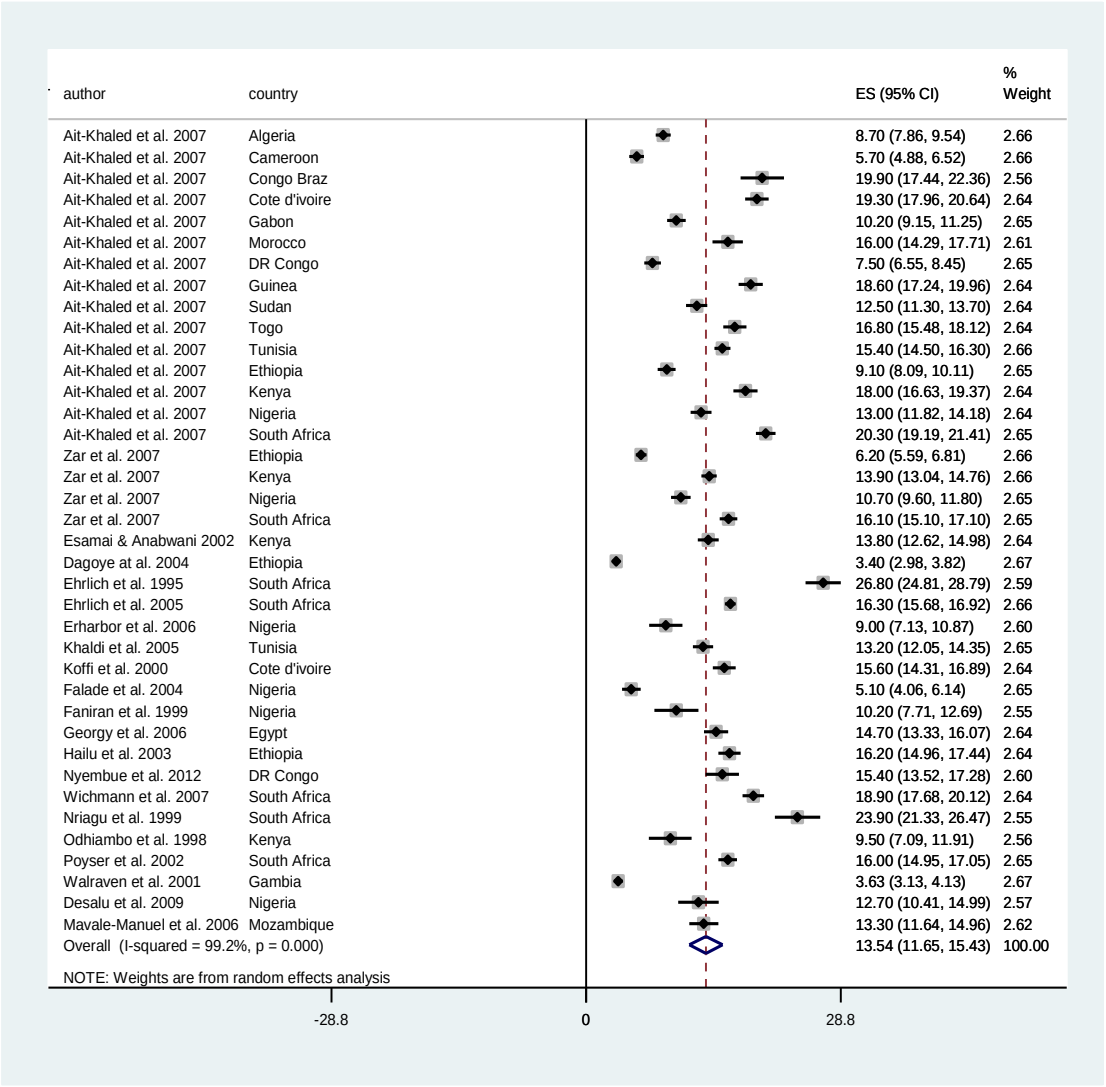

Figure 3.53. Pooled crude prevalence of asthma based on "current wheeze"

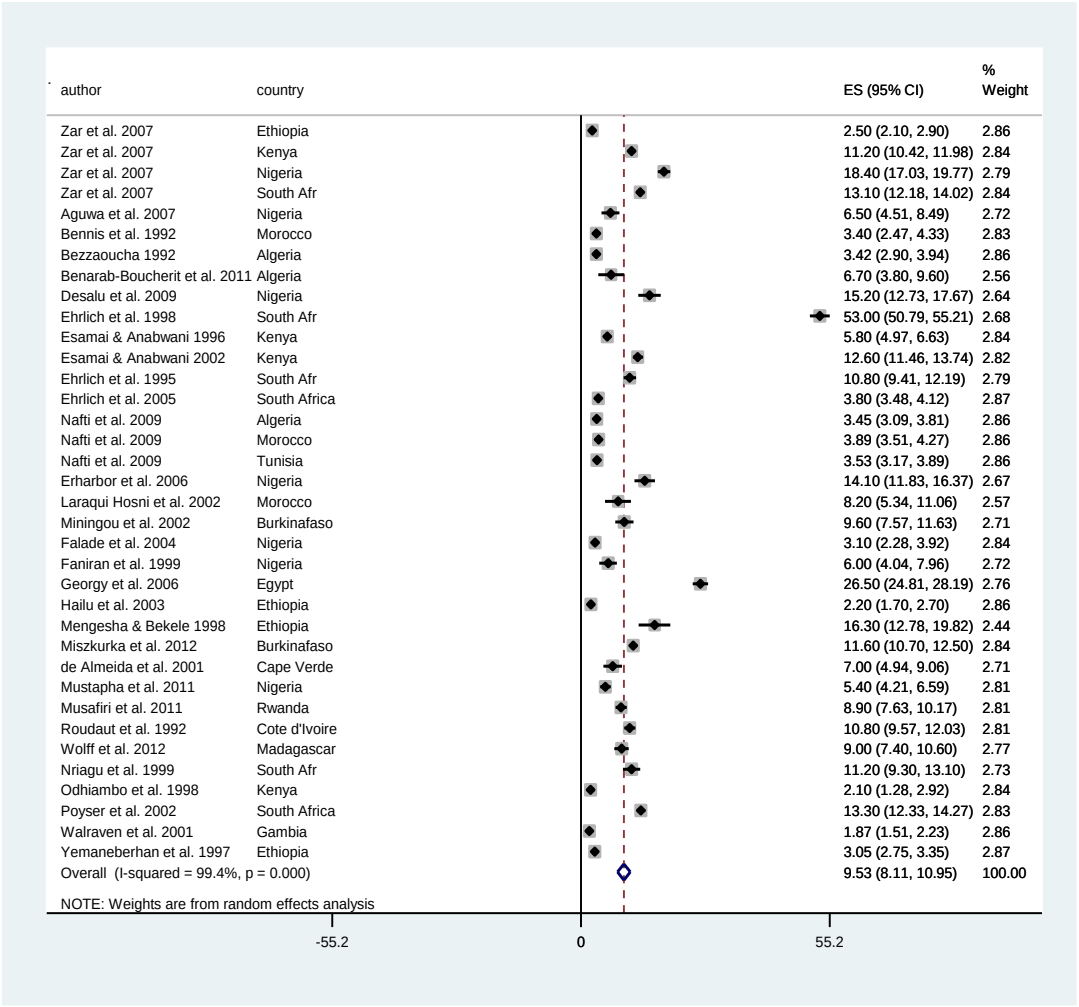

Figure 3.54. Pooled crude prevalence of asthma based on "asthma ever"

It was observed that the pooled crude prevalence rates were consistently higher among urban dwellers than rural dwellers. "Current wheeze" was 9.6% (male 12.1%, female 7.0% (mean age 19.6 years)) in urban settings and 7.0% (male 5.5%, female 3.8% (mean age 17.5 years)) in rural settings. "Asthma ever" prevalence was 5.9% (male 5.6%, female 3.9% (mean age 22.9 years)) and 5.1% (male 4.2%, female 3.1% (mean age 17.5 years)) in urban and rural dwellers respectively (**Table 3.39**).

As noted in the literature review, defining asthma has proved difficult to many researchers and this has limited on-going research efforts globally, especially in Africa. To allow for detailed comparisons of various asthma symptoms, a pooled prevalence of these symptoms that were reported in retained studies have been included in this thesis (**Table 3.40**).

Table 3.39. Asthma prevalence rates among rural and urban dwellers

Asthma indices	***Study setting***	***Study characteristics***		***All***		***Male***		***Female***	
		Study period	**Mean age**	**Data points**	**Prevalence % (95% CI)**	**Data points**	**Prevalence % (95% CI)**	**Data points**	**Prevalence % (95% CI)**
Asthma (ever)	Rural	1993-2008	17.5	6	5.1 (7.2-9.4)	2	4.2 (2.1-6.3)	2	3.1 (0.8-6.2)
	Urban	1993-2010	22.9	7	5.9 (2.9-7.9)	1	5.6	1	3.9
Wheeze at rest (12 month)	Rural	1993-2008	17.5	6	7.0 (2.5-11.5)	2	5.5 (1.4-12.4)	2	3.8 (1.5-12.9)
	Urban	1993-2005	19.6	7	9.6 (3.9-15.2)	1	12.1	1	7

Modelled estimates of asthma prevalence and symptoms in Africa

As noted above, researchers have reported that using the symptoms current wheeze (wheeze at rest- 12 months) yielded better sensitivities from many epidemiological surveys, this is therefore employed in the modelling (See **Appendix 5** for summary of data used in modelling). The modelled prevalence rates and cases of asthma were only estimated for the population under the age of 45 years, as most population groups fall under this age.

In both sexes, there were a total of 29.7 million asthma cases (7.0%; 95% CI: 3.2, 8.5) in children <15 years, and 28.5 million asthma cases (6.2%; 95% CI: 2.6-7.1) among people aged 15-44 years. Among males, there were about 14 million asthma cases (6.5%; 95% CI: 2.8-7.2) in children <15 years, and 16 million asthma cases (7.0%; 95% CI: 3.1-7.7) among males aged 15-44 years. Among females, there were about 14 million asthma cases (7.5%; 95% CI: 3.9-8.7) in children <15 years, and 12.5 million asthma cases (6.2%; 95% CI: 2.5-7.3) among people aged 15-44 years (**Figure 3.55** and **Table 3.41**).

Table 3.40. Pooled crude prevalence rates of reported asthma symptoms from retained studies

Asthma symptoms	***Mean Age (years)***	***Pooled estimate % (95% CI)***		
		Both sexes	**Male**	**Female**
Wheeze at rest (12 month)	15.9	13.5 (11.7-15.4)	13.7 (7.7-14.9))	13.2 (8.1-15.1)
Asthma (ever)*	19.6	9.5 (8.1-10.9)	9.9 (8.9-15.5)	8.1 (8.7-14.3)
Wheeze after exercise (12month)	12.3	23.8 (15.9-31.7)	14.7 (4.4-33.8)	24.6 (11.0-38.2)
Wheeze after exercise (ever)	12.0	8.9 (5.1-12.8)	6.5 (5.3-7.8)	6.5 (4.1-7.9)
Nocturnal wheeze (12 month)	15.4	4.9 (2.4-7.4)	9.1 (7.7-11.1)	10.0 (8.6-11.9)
Nocturnal wheeze (ever)	-	-	-	-
Nocturnal cough (12 month)	14.1	24.2 (18.3-30.0)	24.5 (11.5-37.4)	28.1 (13.2-43.2)
Nocturnal cough (ever)	10.8	9.3 (7.2-11.4)	10.3 (8.1-12.2)	8.5 (6.5-9.9)
Severe wheeze (12 month)	13.1	4.7 (3.7-5.6)	6.0 (4.6-7.4)	3.0 (0.8-5.2)
Severe wheeze (ever)	12.2	8.8 (5.9-11.6)	7.2 (6.0-9.7)	5.2 (4.1-7.3)

**ever* means cumulative prevalence of symptom*

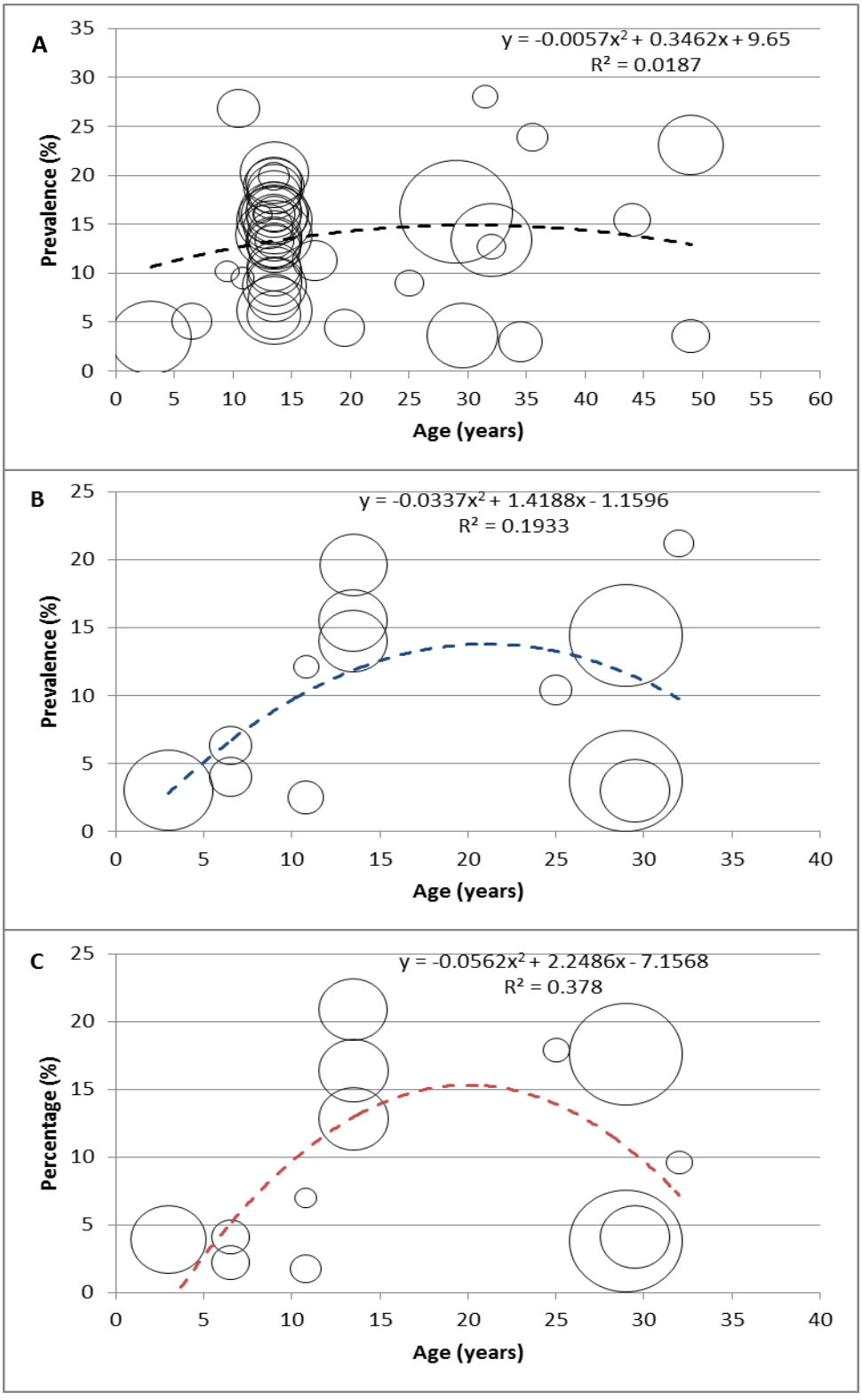

Figure 3.55. Epidemiological model showing distribution of asthma prevalence according to age in Africa in 2010 (A: both sexes, B: male, C: female)

Table 3.41. Modelled estimates of asthma prevalence and cases in Africa in 2010 (derived from epidemiological model and UN population estimates for Africa)

Age (years)	*All*		*Male*		*Female*	
	Prevalence (%)	Asthma cases (000)	Prevalence (%)	Asthma cases (000)	Prevalence (%)	Asthma cases (000)
0-4	3.2	5206	3.8	3132	2.8	2004
5-9	9.2	12809	7.1	5015	10.8	6636
10-14	9.6	11728	9.5	5868	9.9	5389
15-19	9.4	10172	9.9	5405	9.6	4707
20-24	7.7	7378	8.7	4212	7.2	3097
25-29	6.4	5365	7.2	3001	6.1	2172
30-34	4.9	3362	5.8	1983	5.2	1502
35-39	3.1	1726	4.3	1188	2.8	669
40-44	1.0	476	0.8	181	1.5	303
Total (<15)	7.0 (3.2, 8.5)*	29 743	6.5 (2.8, 7.2)	14 016	7.5 (3.9, 8.7)	14 029
Total (15-44)	6.2 (2.6, 7.1)	28 479	7.0 (3.1, 7.7)	15 969	6.2 (2.5, 7.3)	12 451
Total (<45)	6.6 (2.4, 7.9)	58 221	6.8 (2.9, 7.5)	29 985	6.8 (2.7, 7.6)	26 479

**95%CI*

This chapter has provided findings of the systematic review of the four major NCDs: cardiovascular diseases (hypertension and stroke), diabetes, cancers, and chronic respiratory disease (COPD and asthma). From studies reporting prevalence rates, hypertension, with a total sample size of 197734, accounted for 130.2 million cases in 2010. This is followed by asthma, with a sample size of187904, accounting for 58.2 million cases; COPD, with a sample size of 24747, accounting for 26.3 million cases; diabetes, with a sample size of 102517, accounting for 24.5 million cases; and stroke, with a sample size of about 6.3 million, accounting for 1.94 million cases. From studies reporting incidence rates, stroke accounted for 496 thousand new cases in 2010. The overall incidence of the 12 cancer types was higher at 775 thousand new cases, estimated from registry-based data covering a total population of about 33 million. Among women, cervical cancer and breast cancer had 129 thousand and 81 thousand new cases, respectively; and men, prostate cancer and Kaposi sarcoma closely follows with 75 thousand and 74 thousand new cases, respectively (see **Table 3.42**).

Let me state clearly here that the representativeness of all these estimates with regards to the entire African population could not be ascertained. For example, a sensitivity analysis would have given an idea of how truly reflective these estimates are. There are various approaches to conducting sensitivity analysis. One approach is to run the analysis more than once while substituting range of values from studies with arguable eligibility criteria (that is including only studies that are definitely known to be eligible). As noted earlier, until recently, there have not been many studies on NCDs in Africa, and the overall quality of the few studies available is low. In addition, restricting my analysis to studies that have the same study design, same sampling frame and same case definition is also almost impossible. Another approach is to consider median and interquartile range (IQR) of extracted data while observing how these differ from the modelled estimates. Both are then further compared with another set of completely different published estimates on Africa. This approach tends to find arguments in support of the upper and lower limits of my estimate. For example, the incidence of stroke estimated in this thesis (along with the median and IQR) may be compared with another set of published estimates on Africa reporting mortality and case fatality rates. Based on the explanation in *Section 1.1*, where case fatality ratio (CFR) is defined as mortality divided by incidence rate: then, *Incidence rate = Mortality rate/CFR*. This

approach to sensitivity analysis has been applied by Rudan et al. and Nair et al. in the global estimates of clinical pneumonia and Respiratory Syncytial Virus infections in children, respectively (Nair et al., 2010, Rudan et al., 2004). This can also not be conducted in this thesis, as, to the best of my knowledge, there are yet to be such published comparable estimates of NCDs in Africa. However, the median and IQR from the extracted raw data are further shown in **Table 3.42** to allow for some comparisons with the modelled estimates.

Table 3.42. Summary of prevalence/incidence rates and number of cases for the reviewed studies

Disease	***Age***	***Prevalence studies* (%, unless stated)**			***Incidence studies* (per 100000 py)**		
		Cases	**Estimated Prevalence**	**Median (IQR)**	**Cases**	**Estimated Incidence**	**Median (IQR)**
Hypertension	20+ years	130.2 million	25.9 (23.5, 34.0)	30.6 (21.8-36.7)	-	-	-
Stroke	15+ years	1.94 million	317.3/ 100000 (314.0, 748.2)	484 (114-560)	496000	81.3 (13.2, 94.9)	150 (94.5-181)
Diabetes	15+ years	24.5 million	4.0 (2.7, 6.4)	6.2 (2.8-10)	-	-	-
Cervical cancer	All (Women)	-	-	-	129000	28.2 (22.1, 34.4)	26.5 (17.2-41.9)
Breast cancer	All (Women)	-	-	-	81000	17.7 (13.0, 22.4)	18.5 (5.9-23.0)
Prostate cancer	All (Men)	-	-	-	75000	14.5 (10.9, 18.0)	11.5 (4.6-26.0)
Kaposi sarcoma	All (Men)	-	-	-	74000	14.3 (11.9, 16.7)	4.6 (1.9-36.7)
COPD*	40+	26.3 million	-	13.4 (9.4, 22.1)	-	-	-
Asthma	<45 years	58.2 million	6.6 (2.4, 7.9)	13.9 (9.5-16.3)	-	-	-

**No pooled prevalence estimate was reported for COPD due to the limited number of spirometry studies retained (only five) and significant heterogeneity between these studies; estimated COPD cases were only based on median COPD prevalence from retained studies (this has been explained earlier in the methods, and further noted in the study limitations)*

4 DISCUSSION

This chapter is a discussion of the findings from this review, with references to studies that have published similar findings before this review. It also follows the sequence earlier described in the methods and results: cardiovascular diseases (hypertension and stroke), diabetes, cancers, and chronic respiratory disease (COPD and asthma).

4.1 CARDIOVASCULAR DISEASES

4.1.1 Hypertension

This review provides an improved continent-wide estimate of the prevalence and awareness rates of hypertension in Africa using epidemiological modelling adjusted for age and sample size of the respective study population. Having included studies conducted across various parts of Africa, the estimates may provide a close representation of the prevalence and the number of cases of hypertension in the continent.

The IHME GBD study reported an increasing burden of hypertension globally between 1990 and 2010 (Murray et al., 2012, Lozano et al., 2012). Deaths from hypertension increased by 47.8%, from 591 thousand deaths in 1990 to 873 thousand deaths in 2010, while DALYs increased by 37.4%, from 11.2 million DALYs in 1990 to 15.3 million DALYs in 2010 (Murray et al., 2012, Lozano et al., 2012). Generally, this increase cannot be compared directly to the prevalence of hypertension in Africa in the current study, as these are global estimates and the outcome measured were not strictly related to hypertension prevalence. In sub-Saharan Africa however, IHME estimated that DALYs from hypertension increased from 893.6 thousand in 1990 to 1.4 million in 2010 (58.3% increase), while deaths increased by 67.6% from 34600 to 58000 thousand over the same period, respectively (Murray et al., 2012, Lozano et al., 2012). It is also important to state that the sources of IHME data were explored from supplementary files, but there were no data on prevalence of hypertension that could have allowed for further direct comparisons and possibly assist further in estimating the prevalence of hypertension in Africa.

From all studies, I estimated weighted mean systolic and diastolic blood pressures of 129.6 mm Hg and 78.0 mm Hg, respectively, and an overall mean age of 47.4 years. As noted in the methods, the SBP and DBP are only weighted towards the study sample and do not reflect a larger country or regional estimate. For example, most selected studies were conducted in Western Africa and Southern Africa, the overall SBP and DBP may possibly reflect more the high blood pressure status in these regions. However, these may still not be overtly representative of these regions. For example, a South African study had the largest sample size at 11786 (Malaza et al., 2012), and this study was conducted in a rural population known for high HIV prevalence. The estimates reported from this study may be assumed to be confounded by the HIV prevalence and may therefore be difficult to generalize to other African population groups with relatively lower HIV prevalence. Meanwhile, this estimate may still be compared with the estimates reported by Danaei and colleagues on the global trends of systolic blood pressure, with an overall mean SBP in SSA ranging 129.2-132.7 mm Hg and 132.6-134.8 mm Hg among men and women, respectively, between 1981 and 2008 (Danaei et al., 2011). This study may further support my finding of a high prevalence of hypertension in Africa, with the highest value of SBP globally estimated in SSA (along with central and eastern Europe) (Danaei et al., 2011).

Across selected studies, higher prevalence rates of hypertension were reported with increasing age of subjects. This is underpinned by previous research findings where increasing age is associated with significant increase in the prevalence of hypertension, especially in people aged ≥60 years (Anderson, 1999, Addo et al., 2007). A higher prevalence of hypertension was reported in Northern Africa with a pooled prevalence of 33.3% compared to a prevalence of 27.8 % in SSA. This could be partly explained by age difference, with a mean age of 54.3 years in Northern Africa, compared to 46.4 years in SSA. In the 2009 hospital-based Epidemiological Trial of Hypertension in North Africa (ETHNA), a high prevalence (45.4%, mean age 49.2 years) was also reported for Northern Africa (Nejjari et al., 2013); this further supports findings of this study.

A higher prevalence of hypertension was noted among urban dwellers from the pooled estimates mainly in 1990 (urban 17.2%, rural 11.1%), while the prevalence was virtually the same in years 2000 and 2010. The narrowing of prevalence gaps between urban and rural dwellers in years 2000 and 2010 could be due to a possible reverse rural-urban migration, which has been reported when urban dwellers fail to cope with the economic challenges and vulnerabilities associated with urban life, and may prefer to return to natural resource-rich rural settlements (Institute for Security Studies, 2010). In addition, there are reports that even in rural settings, the apparent remote and traditional styles do not seem to protect them again, as more of these rural settings are gradually becoming semi-urbanized (Opie and Seedat, 2005). Opie and colleagues also argued that many site-specific hypertension prevalence estimates in Africa may not truly reflect the burden in these settings, as there are still doubts on the proportion of Africans that truly reside in rural settings (Opie and Mayosi, 2005).

Meanwhile, an increasing, yet low, awareness rate of hypertension in Africa was reported, with pooled awareness rate of 16.9% in 1990, 29.2% in 2000 and 33.7% in 2010. This estimate, to the best of my knowledge, remains the first continent-wide awareness rate of hypertension reported in Africa, and thus forms an important finding of this study. The low awareness rate reported may still reflect a poor response to management of hypertension in the continent (Seedat and Rosenthal, 2006). Kayima et al. corroborates this, reporting a very low awareness rate of hypertension, ranging between 8% and 10% in Africa in the early 2000s (Kayima et al., 2013).

In this review, the general sex distribution showed that the prevalence of hypertension were higher among men than women. This is also in line with many reports in Africa (Kayima et al., 2013, Opie and Seedat, 2005). This may be because the overall mean age from all selected studies was 47.4 years, which is just about a reported mean menopause age of 49.4 years among African women (Ozumba et al., 2004), and there is established evidence of a steeper blood pressure rise in men than women before the age of menopause (Hajar et al., 2006). Danaei and colleagues reported similar findings between 1981 and 2008, where, in contrast to a

predominant rise in mean SBP among men, the mean SBP among women increased only in two countries globally between 1981 and 2008 (Danaei et al., 2011). The current estimate may therefore just be reflective of a continuation in this trend. Still, from the modelling, over 54.6 million cases of hypertension were estimated in 1990 (19.1%), 92.3 million cases in 2000 (24.3%), and 130.2 million cases in 2010 (25.9%). These estimates are higher than the 20 million reported by WHO African regional office (AFRO) in 2005 (WHO Regional Office for Africa, 2005). The WHO AFRO estimate was based on ≥160/95 and this is probably the reason for the low hypertension cases reported. However, reports show that this figure has often been quoted in many official documents as the number of hypertension cases in Africa (WHO Regional Office for Africa, 2006).

As noted in the methods, R-squared (also called the coefficient of determination) is a measure of how close the prevalence rates reported in each study are to the fitted line (Cameron and Windmeijer, 1995). It is defined as the percentage of the response variable variation that is explained by the fitted line (Cameron and Windmeijer, 1995). It is usually between 0 (indicating that the model explains none of the variability of the plotted data around its mean) and 100% (indicating that the model explains all of the variability of the plotted data around its mean) (Cameron and Windmeijer, 1995). In other words, the higher the R^2 the better the model fits the plotted data. For the hypertension modelling, an exponential, non-linear model was applied (other models in this thesis are also non-linear, see *methods*). The R^2 for the three years (1990, 2000 & 2010) were less than 50%, ranging from 6%-37%; this may apparently mean that the model does not fit the data well. However, according to some authors, a low R^2 may not mean the model is not well-fitted (Oles et al., 2012) (Cameron and Windmeijer, 1995). Some have argued that R^2 does not indicate whether a model is adequate, and in such instances a good model may present with a low R^2 and a poor model may have a high R^2 (Higgins et al., 2009). In fact, many have reported that R^2 is more appropriate for linear regression (Oles et al., 2012, Higgins et al., 2009). In a typical linear regression, the variance is approximately equal at every point along the scale, hence, the sum of regression sum of squares (SSR) and sum of squared deviations (SSD) is always equal to total sum of squares

(SST) (i.e. *SST=SSR+SSD*) (Cameron and Windmeijer, 1995). According to experts, this is quite logical, as the variance that the linear regression model accounts for, and the error variance adds up to equal the total variance (Cameron and Windmeijer, 1995). Based on this therefore, R^2 is calculated as:

$$R^2 = 1 - (\text{regression sum of squares} / \text{Total sum of squares}), \text{ OR } 1-(SSR/SST)$$

As noted above, this equation must arithmetically produce values between 0 and 100% in a straight-forward linear regression. According to statisticians, this linear R^2 equation is what is usually available in many statistical packages. Making inferences from this R^2 in a non-linear model may therefore be misleading. In a non-linear model, the sum of regression sum of squares (SSR) and sum of squared deviations (SSD) is not always equal to total sum of squares (SST) (i.e. $SST \neq SSR+SSD$), as the underlying assumptions are completely different from a linear model. Thus, R^2 for non-linear models may not actually fall between 0 and 100%, there may be negative figures (Cameron and Windmeijer, 1995, Oles et al., 2012). Spiess and Neumeyer performed over a thousand simulations to show that using R^2 to evaluate the fit of non-linear model may lead to inaccurate deductions (Spiess and Neumeyer, 2010). They found out that: (*i*) R^2 tends to be consistently high for both very bad and very good models; (*ii*) even with improved non-linear models, R^2 do not always increase; and (*iii*) using R^2 to choose the final model only gave a representative prediction in about 28 to 43% of analyses (Spiess and Neumeyer, 2010). The question then is what form of R^2 should then be used for non-linear regression (like applied in this thesis)? Again, statisticians reported that there is no straightforward R^2 for non-linear regression (Cameron and Windmeijer, 1995). Quasi (or pseudo) R^2 has been applied in some advanced statistical modelling, which tends to adjust for the non-linearity in the model. However, as noted in the *introduction* and *methods*, this thesis is based on simple modelling, particularly due to paucity of data on many NCDs in Africa and widespread concerns about extrapolation and over-modelling of the scarce data in Africa in other studies. Hence, I did not apply an advanced modelling with a quasi (or pseudo) R^2 in my analysis. There are, however, varying forms of pseudo R^2 that

can be applied in a non-linear model. One approach is a form of generalization of the R^2 formula, which approximates the usual R^2 using multiple regression analysis.

> *Quasi R-Squared = (ModelSS - MeanSS)/(TotalSS-MeanSS)*
>
> where MeanSS is the sum of squares due to the mean, ModelSS is the sum of squares due to the model, and TotalSS is the total (uncorrected) sum of squares of Y (the dependent variable) (Spiess and Neumeyer, 2010).

In this approach, the R^2 may explain how well the non-linear model performs after removing the influence of the mean of Y. The limitation here is that many non-linear models may not clearly include a parameter for the mean of Y; therefore, the R^2 may be negative, and in this case, the statistical package will set the R^2 to zero, thus rendering it difficult to interpret (Spiess and Neumeyer, 2010).

Another approach to calculating R^2 is to square the correlation between the actual *y* values and the predicted *y* values (Cameron and Windmeijer, 1995). This approach may only be useful as long as the model is close to a linear model (Cameron and Windmeijer, 1995). In fact, the ability of any quasi R^2 to accurately predict a good fit has been said to be based on the closeness of the model to a linear model. This thus still explains why some statisticians do not rely on any form of R^2 to interpret a non-linear model (Spiess and Neumeyer, 2010, Cameron and Windmeijer, 1995).

Meanwhile, a close look at the model shows an increasing trend in hypertension prevalence from 20 years to 80+ years: 12.5% to 35.7% in 1990, 17.5% to 55.1% in 2000, and 16.4% to 75.7% in 2010. Increasing age has been reported as a major risk factor for hypertension and many other chronic diseases (Ejim et al., 2011). The overall prevalence also increased from 19.1% in 1990 to 25.9% in 2010. While I understand that there are lots of demographic factors that can affect these estimates, the pattern presented by the model may not be too far from what is happening in the African population, especially with regards to the rise in prevalence of hypertension with increasing age, which has been reported by researchers (Ejim et al., 2011). Epidemiologists have explained that in the application of a model for data analysis, it

is important not only to look at the R^2 and how well the model fits the data, but also to closely examine if the model is a reasonable prediction in a scientific context, which in this case may be linked to published evidence on increasing age and the prevalence of chronic diseases (Spiess and Neumeyer, 2010).

Meanwhile, Twagirumukiza et al. estimated about 75 million cases (16.2%) of hypertension among people aged ≥15 years in SSA in 2008, and projected to increase to 125.5 million cases (17.4%) in 2025 (**Table 4.1)** (Twagirumukiza et al., 2011). While I did not provide prevalence estimates beyond 2010, however, going by population demographics and ageing alone, these figures are relatively lower compared to the current estimates. It is understandable that these estimates were for SSA and that the mean age of the study was low (40 years), they may still yet not reflect the true burden of hypertension in the continent, as their review and analysis mainly included studies from 11 countries in Africa. Another reviewer further noted my concerns, and agreed the estimates were very low compared to recent prevalence rates reported in Africa, and may be erroneously interpreted that the burden of hypertension in the continent is low (Poulter, 2011). However, Kearney et al. reported higher hypertension estimates, with about 79.8 million hypertension cases (27.6%) estimated among people aged ≥20 years in 2000 and projected to reach about 150.7 million cases (27.7%) in 2025 (Kearney et al., 2005), see **Table 4.1**. These prevalence rates are comparable with the current estimates, but as noted above, the difference in the number of hypertension cases may be due to the fact that I considered the UN demographic changes in my overall estimates.

Table 4.1. Comparable estimates of hypertension prevalence rates from selected studies

	Current Study *		***Kearney et al. * (6)***		***Twagirumukiza et al. ** (15)***	
	2000	2010	2000	2025	2008	2025
Prevalence rate in % (95% CI)	24.3 (23.3, 31.6)	25.9 (23.5, 34.0)	27.6	27.7	16.2	17.4

**20years (all Africa), **15+years (sub-Saharan Africa)*

Study limitations

The study aimed to provide an improved continent-wide estimate of hypertension in Africa using current definitions (≥ 140/90mm Hg), however, there are a number of factors that could have limited this. First, the modelling was age-dependent, as there are other health determinants that could have resulted in varying estimates if considered, including the overall population characteristics, socio-economic factors and general living conditions (Negin et al., 2011). I already noted in the methods that single age (usually mean age) was mostly employed in the modelling. There were only 6 studies out of the 92 selected studies (6.5%) that reported age-specific prevalence estimates that were employed in the modelling (Abegunde and Owoaje, 2013, Hendriks et al., 2012, Fezeu et al., 2010, Edwards et al., 2000, Cruickshank et al., 2001, de Ramirez et al., 2010). This thus means that hypertension prevalence of people in the extreme age groups (very young and very old) may not be well represented when the mean age was only employed. This is therefore a major limitation in this study.

I^2 is the measure of heterogeneity reported in this thesis, and was first described in the Cochrane Reviews. I^2 describes the percentage of total variation across studies that are due to heterogeneity rather than chance. For the hypertension pooled prevalence, I^2 was 99.5%. This implies that there is very high heterogeneity across selected studies; and at $p<0.0001$, the heterogeneity is statistically significant. There is therefore strong evidence against the null hypothesis that studies are evaluating the same effect. For a combination of studies with such high heterogeneity, it may not be appropriate to pool a summary effect. However, as reported earlier, there is very low research output in Africa, and the few studies have not been conducted under strict international guidelines, so heterogeneities can be expected. In addition, restricting my analysis to studies that have the same study design, same sampling frame and same case definition is almost impossible. However, despite this high heterogeneity, it is important to note that the overall quality check employed involved closely examining individual study designs, analyses, case definitions, and the generalizability of the estimates to a larger African population group.

In addition, the overall mean age was 47.4 years, which could also have resulted in a lower prevalence estimate, as research evidences show significant increase in hypertension prevalence in people aged ≥60 years (Anderson, 1999). Second, all studies included in our modelling were based on ≥140/90mmHg and/ or self-reported use of antihypertensive medications; notwithstanding, some studies have varying designs and blood pressure measuring protocols, which could have affected the quality of the current estimates. Moreover, while I ensured all studies that were graded as *high* and *moderate quality* were included in the quantitative analysis, some *low quality* studies were also included in the quantitative analysis on the basis of good study designs; I think this could potentially affect the overall estimates. Third, not all studies reported age- and sex- specific estimates, including urban or rural site-specific estimates, as an epidemiology of the prevalence of hypertension in these sub-groups could have been further helpful. Furthermore, the incompleteness of data across many studies prevented me from providing estimates on the control and treatment of hypertension in Africa; I still hope that providing a continent-wide estimate of the awareness rate of hypertension may further give a general view of the public health response to the disease in the continent. Lastly, despite including 92 studies conducted in 31 African countries and with a consideration of the United Nations population demographics in the modelling (refer to **Table 3.2** and **Appendix 2)**, I still cannot say with all certainty how closely representative my estimates were of the African population.

Public health response to hypertension in Africa

Recent reports show that the World Heart Federation, supported by the Pan African Society of Cardiology (PASCAR), has been actively building capacities across Africa to address the rising burden of hypertension and other cardiovascular diseases in the continent (World Heart Federation, 2008). However, collaborations and response within Africa remains poor, as hypertension still ranks low among health priorities, owing to competition for the limited resources from a co-existing high burden of infectious diseases (Beaglehole et al., 2011). Moreover, in countries with some levels of care for hypertension, the standards of health service delivery is poor (Opie and Seedat, 2005). Many cases of hypertension are detected late, treatments rarely follow standard guidelines, and the costs of medications are generally high (Hajar et al., 2006). Besides, health care seeking behaviour has also been affected, with people often preferring low-cost substandard health facilities (Suhrcke et al., 2012). This is particularly a problem in rural settings where the prevalence of hypertension has been reported to be on a gradual increase (Kayima et al., 2013). Further reports show that even with a relatively lower prevalence of hypertension among rural dwellers, the detection and overall management are poor in comparison to urban dwellers (Opie and Seedat, 2005). Additionally, many African countries are yet to implement population-wide control measures to address risk factors for hypertension (van der Sande et al., 2001), even with confirmed reports of high salts and fats consumption in the region and evidence showing cost-effectiveness of interventions targeting this (Mezue, 2013, Gaziano et al., 2005). The WHO now recommends country-specific initiatives and legislation concerning food labelling and products formulation, including sodium and saturated fats content in processed foods (World Health Organization, 2013b, World Heart Federation, 2008).

This study suggests a high prevalence of hypertension in Africa, and the awareness of the disease, though increasing, still remains low. Hypertension deserves to be on the health priority lists of African nations, and problems with funding may possibly be reduced by partnering with leading international bodies for cardiovascular diseases. Essentially, policy makers and stakeholders in the health sector need to

institute nationwide population-based strategies towards creating awareness on hypertension and educating people on the main risk factors such as smoking, harmful use of alcohol, sedentary lifestyles and unhealthy diets. It is hoped that the findings of this review may prompt appropriate policy response at country level towards improved detection, control and overall management of hypertension in Africa.

4.1.2 Stroke

Some systematic reviews have been published on the burden of stroke in Africa but without a continent-wide estimate of stroke incidence and prevalence rates (Connor et al., 2007, Kengne and Anderson, 2006). There are also global reviews of stroke with few studies on Africa population included (Feigin et al., 2009, Feigin et al., 2003, Aho et al., 1980). For example, in a systematic review of 56 population-based studies globally, only one African site (Ibadan, Nigeria) was considered. The result from this survey may not necessarily reflect the overall burden of stroke in Africa (Feigin et al., 2009). However, to the best of my knowledge, this study provides the first continent-wide estimate of the incidence and prevalence rates of stroke in Africa. The estimates were based on an epidemiological model with appropriate consideration of reported mean ages and sample sizes from individual studies. One important thing about this review was that despite the few studies retained, the estimates provided in this study were based on a total sample size of about 6.3 million. Moreover, having applied the UN population demographics in the final model, the current estimates fairly reflect the total African population and may help policymakers across several African countries institute effective public health response to the growing burden.

Generally, crude incidence rates of stroke from population/community based-studies were higher, with the two low incidence rates recorded obtained from population-based stroke registries in Nigeria (Danesi et al., 2013, Osuntokun et al., 1979) (**Table 3.12**). Despite over 3 decades of potential improvement in stroke registration between the two studies (1975-2007), the low incidence rates may still be indicative of incompleteness of stroke registries in many Africa settings, and that data obtained from these registries may be unreliable and inappropriate for estimation of stroke burden. In contrast, in many high income countries where there is active registration of stroke cases, population-based stroke registries have been reliable sources of data for estimation of stroke incidences (Connor et al., 2007, The Global Burden of Disease Stroke Expert Group, 2012).

In this study, the pooled crude incidence rate from community-based studies was higher at 112.9 per 100,000 person years compared to 77.4 from hospital-based studies. The difference suggests a likely under-estimation of stroke incidence rates from hospital-based studies, which has also been observed by some previous studies, particularly due to the very few stroke cases presenting to standard health facilities (Chin, 2012). The observed prevalence rates of stroke survivors were generally high (all prevalence studies were population-based) with a pooled crude prevalence rate of 387.9/100,000 population. The low prevalence rate recorded in Ethiopia in 1988 may not be unconnected with the high mortality rates from stroke in the region, which has generally been reported in many parts of Africa (Tekle-Haimanot et al., 1990, Bonita and Truelsen, 2003).

The modelling showed a rising incidence and prevalence rates of stroke with increasing age and higher figures recorded among men, which is in line with several research findings on stroke burden (Dewhurst et al., 2013a). Over 496 thousand new cases of stroke with an incidence rate of 81.3/100,000 py (men 103.4, women 59.6), and about 1.94 million stroke survivors with a prevalence rate of 317.3/100000 population (men 335.2, women 299.7), both among people aged 15 years or more were estimated in 2010. In the modelling applied for stroke, the R^2 for both incidence and prevalence of stroke were above 50%, at 66% and 71% respectively. These are relatively high values, but just as explained earlier under *hypertension discussion*, this may not necessarily imply that the model fits the data very well (Oles et al., 2012). The model shows an increasing trend from 15 years to 80+ years: 7.3 to 1601.3 per 100,000 person years (incidence), and 35.2 to 5324.5 per 100,000 populations (prevalence). The fact on age still applies here: increasing age has been reported as a major risk for many NCDs (Hammami et al., 2011). While this model may reflect some intrinsic population characteristics with regards to age and occurrence of stroke in a population, there is still need to be aware of other intrinsic population characteristics related to stroke that are not explained by this model especially on correctly identifying first and recurrent cases of stroke. Additionally, the inability to appropriately account for urbanization and many NCD risk factors are also important factors that must be considered. Largely, examining R^2 and how well

the model fits the data may not be the most important thing in data analysis, but also to closely examine if this is a reasonable prediction in a scientific context (Cameron and Windmeijer, 1995).

Meanwhile, a report in 2004 suggested that about 8% of all first-ever strokes (about 5 million) occurred in Africa and 5% of over 30 million stroke survivors worldwide were in Africa (Truelsen, 2010b, World Health Organization, 2004), and this amounts to about 400 thousand new stroke cases and 1.5 million stroke survivors. A systematic review in sub-Saharan Africa on studies published between 1966-2006 showed age-standardized prevalence rates of 114–315/100,000 populations and 154–281/100,000 population among men and women, respectively (Connor et al., 2007). Another review in 2006 showed that the prevalence of stroke survivors ranges from 200-300/100,000 population in sub-Saharan Africa, and incidence rates ranges from 15-68/100,000 py (Kengne and Anderson, 2006). These figures are comparable with the current estimates, which further underpins a near representation of the burden of stroke in Africa. The few differences may probably be due to the study periods, age groups, fewer data-points, focus on sub-Saharan Africa, and the fact that these were largely qualitative reviews and not based on a detailed statistical synthesis.

Meanwhile, according to the GBD estimates by Feigin and colleagues, over a 100% increase in the total number of new stroke cases and stroke survivors was recorded between 1990 and 2010 in LMIC, with an estimated incidence rate of 281.1/100,000 py and prevalence rate of 393.4/100,000 population in 2010 (Feigin et al., 2014). While it is understandable that not all LMIC have contextual similarities with African countries and direct comparisons may be inappropriate, it may however still be logical to conclude that the estimates from this study reflect the current stroke burden in many LMIC. In sub-Saharan Africa however, IHME estimated that DALYs from stroke increased from 5.9 million in 1990 to 7.8 million in 2010 (32.2% increase), while deaths increased by 47.0% from 223.8 thousand to 328.9 thousand over the same period, respectively (Murray et al., 2012, Lozano et al., 2012).

Study limitations

While this study aimed to provide an evidence-based continent-wide estimation of stroke incidence and prevalence rates in Africa through simple statistical analysis, the study has some important limitations. The modelling was strictly based on age. As noted in the methods that single age (usually mean age) was mostly employed in the modelling. However, of the 19 studies selected, 9 studies (47.4%) reported age-specific prevalence estimates that were employed in the modelling (Connor, 2004, Cossi et al., 2012, Danesi et al., 2007, Danesi et al., 2013, El Tallawy et al., 2013, Farghaly et al., 2013, Kandil et al., 2006, Walker et al., 2010, Osuntokun et al., 1979). This thus means that stroke prevalence and/or incidence of people in the extreme age groups (very young and very old) may not be well represented from the other studies that the mean age was only employed. This could therefore a major limitation in this study. In particular the low research output and quality of selected studies from Africa constrained the overall analysis. There were 19 studies covering only 10 countries in Africa with an overall sample size of over 6.3 million. Moreover, stroke case ascertainment was not well defined across some studies, and this has been documented in some reviews (The Global Burden of Disease Stroke Expert Group, 2012). Due to these limited data and with some full texts assessed showing evidence of a detailed epidemiological exercise, an inclusion of some of these studies in the final analysis was allowed, as contained in the quality criteria and grading. In addition, some reported stroke incidence data were based on both first stroke and recurrent stroke events, and not all reported prevalence rates were strictly based on stroke survivors. Importantly, this study could have been limited by the inability to account for the consequences of stroke on conditions other than acute stroke, as a wide range of overt and occult cerebrovascular disease have been recognised to contribute to Alzheimer's disease, vascular dementia and other cognitive disease (O'Neill, 2014). Diseases under this category may therefore be unaccounted for.

For the pooled stroke estimates, I^2 was 97.5% for incidence rate, and 98.8% for prevalence rate. This thus implies that there is very high heterogeneity across selected studies; and at $p<0.0001$, the heterogeneity is statistically significant. There is therefore strong evidence against the null hypothesis that studies are evaluating the

same effect. For a combination of studies with such high heterogeneity, it may also not be appropriate to pool a summary effect. However, as reported earlier, there is very low research output in Africa, and the few studies have not been conducted under strict international guidelines, so heterogeneities can be expected. In addition, restricting my analysis to studies that have the same study design, same sampling frame and same case definition is almost impossible. Lastly, I cannot say with all certainty how closely representative these estimates were of the larger African population (refer to **Table 3.10** and **Appendix 3**).

Public health response to stroke in Africa

The prevention of stroke and many non-communicable diseases in Africa has been affected mainly by weak health systems and poor government response (Bonita and Truelsen, 2003). To date, the priorities of many African countries remain infectious diseases: mainly HIV/AIDS, malaria and tuberculosis (Beaglehole et al., 2011), despite the availability of affordable and cost effective stroke prevention initiatives (Walker et al., 2013, Mensah, 2003). For example, Walker and colleagues reported that African countries do not have national strategies to address smoking, alcohol, physical inactivity and unhealthy diets including reducing salt and fat contents of processed foods (Walker et al., 2013); and stroke units, where the awareness on these risk factors could have been raised, are rarely available (Wahab, 2008, Kolapo and Vento, 2011). The INTERSTROKE study findings show that hypertension is the main risk factor of all stroke subtypes with odds of about 2.64 (O'Donnell et al., 2010), this is more prominent among young Africans who present with stroke unaware of their high blood pressure status (Walker, 1994). Truelsen argues that the prevalence of stroke in Africa might increase due to substantial changes in major stroke risk factors in the presence of a biased focus on the prevention and control of infectious diseases, at the expense of many NCDs (Truelsen, 2010a).

The diagnosis of stroke in many African settings remains a huge challenge (Kengne and Anderson, 2006). Some hospital surveys in sub-Saharan Africa have shown that CT scans are only conducted on less than half of patients presenting with stroke, and this is mainly among those that can afford it (Kengne and Anderson, 2006,

Olubunmi, 2007). In fact, experts have reported that the unavailability and/or high costs of cranial CT imaging in many parts of Africa have limited information on the pathologic profiles of different stroke types in the continent, with this often affecting the diagnosis, treatment and the overall management of the disease (Olubunmi, 2007). Reports further show that in some areas with better population-wide access to CT scans, as the case in Tanzania, Ghana, and the Medical University of Southern African (MEDUNSA) Stroke Data Bank (MSDB), there have been improvements in diagnosis of stroke, with varying cases of ischaemic and haemorrhagic strokes reported (Joubert, 1991, Matuja et al., 2004, Nyame et al., 1994). Moreover, the challenges of appropriately distinguishing first from recurrent stroke episodes have also affected stroke case ascertainment, especially during epidemiological surveys (Connor et al., 2007) Neurologists have noted the importance of proper planning during community surveys, active registration and follow-up of new stroke cases identified, and training and re-training of health workers on stroke diagnosis (Sudlow and Warlow, 1996); arguing that the absence of these in many African settings have resulted in increased number of stroke cases in the community who have never had contact with standard health facilities, and inability to categorize these as first or recurrent strokes, including relating such existing stroke cases to a particular period during surveys (Sudlow and Warlow, 1996, Connor et al., 2007).

As noted earlier, a systematic review has suggested that income is a strong predictor of stroke risk and fatalities (Johnston et al., 2009). For example, the average cost of a cranial CT in Uganda was approximately $60 USD between 2000 and 2010 (Chin, 2012). This is expensive in most African population groups where many still live below the poverty index of less than $1.25/day (World Bank, 2014a). In fact, the high cost of health services in the absence of an effective health insurance schemes and adequate resources allocated for stroke prevention and management has affected healthcare seeking behaviour in some African settings (Connor et al., 2007, Walker et al., 2000). Many stroke patients have been managed at home due to lack of hospital funds, with only few presenting to standard health facilities several days after the onset of symptoms having tried low-priced under-resourced clinics (Chin, 2012). For those who manage to get to standard health facilities, there are also

challenges arising from poor quality of care, as several studies have reported massive gaps exist in the management of acute stroke in Africa compared to many high income countries (Lemogoum et al., 2005, Adoukonou et al., 2010).

The unavailability of data with low research output has been a major setback in the management of stroke in Africa (Truelsen, 2010a). Experts have reported that reliable data from which evidence-based policy decisions can be made are sparse in Africa (Owolabi, 2012). For example, in an attempt to quantify number of publications on stroke up till 2009, Holmes and colleagues reported that there were 14 population-based cross-sectional studies on stroke in Africa, accounting 0.06 studies per million people with stroke in Africa, and this only representing 0.6% of the total publications on stroke in the United States (Holmes et al., 2010). Many have argued that no study in Africa can be regarded as an ideal stroke study (Sudlow and Warlow, 1996), adding that there were no proper stroke registries and demographic health surveys which invariably limit active registration, follow-up of cases and conduct of community-based studies (The Global Burden of Disease Stroke Expert Group, 2012). Based on the current findings, hospital-based studies and door-to-door surveys were mainly conducted in Africa and despite the rigour of these few epidemiological surveys, gaps have been identified with regards to case ascertainment and study protocols (Bonita and Truelsen, 2003).

The findings in this study suggest an increasing burden of stroke in Africa. However, with the current low availability of data, there is still need for more research on stroke, and related vascular disease risk factors to appropriately quantify this burden. An investment in research capacity, basically to conduct and fund higher quality research may help raise awareness on stroke burden in Africa. An awareness and fair understanding of stroke burden and disease pattern in Africa may further prompt appropriate policy response and scale up current intervention programmes.

4.2 DIABETES

In the current analysis, statistical methods were employed involving pooling diabetes prevalence from all studies, and applying the epidemiological model, while considering the mean ages and sample sizes of the respective study population. As noted in preceding sections, epidemiological surveys have revealed significant association between the prevalence of many NCDs and age of patients (Beaglehole, 2011). Besides, by using the UN demographics, this study may have considered effects of urbanization, changing population dynamics and increased life expectancies on the prevalence of diabetes in Africa. The current figures could represent a realistic estimate of the prevalence and number of cases of diabetes in Africa.

Across individual studies, higher prevalence rates of diabetes were reported in Northern Africa. Although the very high prevalence (38.4%) observed in Morocco may not be plausible, as diabetes was surveyed alongside other cardiovascular risk factors, and the case definitions and study population were not well defined (Essiarab et al., 2011).

Meanwhile, DR Congo and Seychelles had the highest prevalence of IGT and IFG across selected studies, with a diabetes prevalence of 10.0% and 11.7 % respectively. Interestingly, the two countries had high prevalence of diabetes, with a diabetes prevalence of 10% in DR Congo and 11.5% in Seychelles. This finding (high IGT and IFG prevalence with a relatively high diabetes prevalence) may suggest that the two countries are at the early phase of diabetes epidemic, which further supports the findings reported by Mbanya and colleagues (Mbanya et al., 2010). Additionally, from the pooled estimates of IGT and IFG across all studies, a higher prevalence of IGT was observed among women, while IFG was more prevalent among men (**Table 3.17**). This pattern has also been reported by WHO, but experts can still not say with certainty the reason for this (World Health Organization, 2006).

On the study settings, several reports have shown positive association between diabetes and urban areas (Aspray et al., 2000, Levitt, 2008, Mbanya and Ramiaya,

2006). Sobngwi et al. estimated a diabetes prevalence of 1% in rural Africa and 2%-6% in urban Africa in 2002 (Sobngwi et al., 2002). In the current study, there was no test of association between the study settings and diabetes prevalence rates. However, the pooled estimates revealed a 4 fold increase in diabetes prevalence among urban dwellers (10.1%) compared to rural dwellers (2.6%) (**Table 3.19**). This is in line with many previous reports and is believed to be due to increase risks of NCDs associated with urban life, as noted in the introduction (Mbanya et al., 2010).

Based on the current study, a pooled diabetes prevalence of 7.5% was estimated from crude prevalence rates reported in all studies. Varying degrees of heterogeneities from some of these studies including those related to individual population structure, residence (differences between urban and rural areas), mean age and other social determinants of health, that were ignored or not fully accounted for in the random effects analysis, could have possibly resulted in this high estimate (and vice-versa).

However, as noted in the methods, the epidemiological model incorporated the age and sample sizes which only relatively represent some features of the study population (and not the larger regional or country population). Estimated figures from this model showed an increasing prevalence of diabetes since 1990, with marked increase noted between 2000 and 2010; this agrees with findings of other studies conducted in Africa where an increasing prevalence has been documented over the last three decades (Mbanya et al., 2010, Levitt, 2008, Beran and Yudkin, 2006). Meanwhile the reported high prevalence of undiagnosed diabetes also reflects the current low level of response to the disease in Africa. This finding may therefore support the view that many people in Africa with diabetes still remain unaccounted for (Sobngwi et al., 2001, Mbanya et al., 2010).

From the modelling, it was observed that the prevalence of diabetes and absolute number of cases in females were rising at a faster rate compared to males, with the female prevalence actually higher than male prevalence in 2000 and 2010. This may reflect concerns of some experts who have noted an increase in metabolic syndrome among females, especially in many LMIC (Mbanya et al., 2010). It may also point to an increasing prevalence of overweight and obesity among African women, which

are prominent risk factors for diabetes and many NCDs (Beaglehole, 2011, Mbanya and Ramiaya, 2006). In fact, obesity is even now more prevalent among African women as this relatively portrays a wealthy status (Mbanya et al., 2010).

On the properties of the model, the R^2 for the three years (1990, 2000 & 2010) was less than 50%, ranging from 23%-37%. This may mean that the model does not fit the data well. The estimates should therefore be cautiously interpreted. However, some authors have stated that a low R^2 may not mean the model is not well-fitted (Cameron and Windmeijer, 1995). A detailed discussion on R^2 has been included earlier under *hypertension discussion*. The model shows an increasing trend in diabetes prevalence from 15 years to 80+ years: 0.7% to 21.7% in 1990, 1.3% to 15.2% in 2000, and 1.6% to 24.4% in 2010. The overall prevalence also increased from 2.4% in 1990 to 2.9% in 2000 and 4.0% in 2010. As noted above, increasing age has been reported as a major risk for chronic diseases, including diabetes (Mbanya et al., 2010). However, this model may need to be cautiously interpreted especially with the ongoing rapid epidemiological transition across Africa. The inability to appropriately account for urbanization and many NCD risk factors are also important factors that must be considered. As noted, it is important not only to look at the R^2 and how well the model fits the data, but also to closely examine if this is a reasonable prediction in a scientific context (Cameron and Windmeijer, 1995).

Meanwhile, increasing prevalence of diabetes was observed in the last two decades from the modelled estimates, with an estimated diabetes prevalence of 2.4% in 1990 increasing to 4.0% in 2010, this accounting for 40% increase in diabetes prevalence between 1990 and 2010. These figures are comparable with findings from other studies, with an estimated diabetes prevalence of 3.8% (Shaw et al., 2010), and 5% (Whiting et al., 2011), both reported by IDF for the year 2010 estimates. In South Africa, which many reviews have suggested has the highest diabetes prevalence in sub-Saharan Africa (Mbanya et al., 2010), a systematic review reported a prevalence of 5.5% among people aged ≥ 30 years (Bradshaw et al., 2007), this estimate is not too different from the estimate in the current study. On the number of diabetes cases, 8.5 million diabetes cases were estimated in Africa among people aged ≥15 years in

1990, 13.5 million in 2000, and 24.5 million in 2010. The higher estimates in this study (in comparison to previous reports) may be due to ageing and population growth (reflecting from the UN population demographics employed in the modelling), and failure to account for over-representation of studies with high diabetes prevalence, for example from urban areas where diabetes prevalence is higher. Looking at previous reports, Wild and colleagues estimated about 7.1 million people living with diabetes in sub-Saharan Africa in 2000 and projected to increase to 18.6 million by 2030 (Wild et al., 2004); Shaw and colleagues reported a prevalence of 12.1 million diabetes cases in Africa in 2010 and projected to increase to 23.9 million by 2030 (Shaw et al., 2010); while Whiting and colleagues estimated 14.7 million diabetes cases in Africa in 2010 and projected to increase to 28 million by 2030 (Whiting et al., 2011), see **Table 4.2**.

In sub-Saharan Africa however, IHME estimated that DALYs from diabetes increased from 2.3 million in 1990 to 4.3 million in 2010 (87% increase), while deaths increased by over 100% from 61.1 thousand to 123.7 thousand over the same period, respectively (Murray et al., 2012, Lozano et al., 2012).

Table 4.2. Estimated diabetes prevalence and cases in Africa from different studies

Year	*Current study**	*Wild et al.†*	*Shaw et al.*†*	*Whiting et al.*†*
1990	8.5 million (2.4% (0.9, 4.1))	7.1 million	-	-
2000	13.5 million (2.9% (1.7, 3.9))	-	-	-
2010	24.5 million (4.0% (2.7, 6.4))	-	12.1 million (3.8%)	14.7 million (5.0%)
2030	-	18.6 million	23.9 million (4.7%)	28 million (5.9%)

**Africa (15+ years), †sub-Saharan Africa (all population), *†Africa (20-79 years)*

Based on these studies (**Table 4.2)**, from 2004 to 2011, the authors reported different, yet higher diabetes cases and prevalence rates, for the same reviewed year, across the three studies. Just as observed from my estimate, this may reflect availability of more data, improved study designs and consideration of demographic changes in the continent. However, the two recent studies of Shaw et al. and Whiting et al. (conducted in collaboration with the IDF atlas committee) were conducted across the whole African continent, but were based on ages 20-79 years. The difference in reported estimates of the two studies, within one year separating both studies (2010 and 2011), could also point to the fact that newer reports may give fairly higher and close estimates of the prevalence of diabetes in Africa, and this argument has been noted in several reviews (Sobngwi et al., 2001, Mbanya et al., 2010).

Meanwhile, based on **Table 4.2**, the number of diabetes cases in Africa reported in the current study was almost double those reported by IDF in 2010 and 2011. Asides the fact that the IDF estimates were reported for people aged 20 to 79 years, the current estimates (though based on age 20 years and above) may still not be plausible. One main reason is that the epidemiological model did not account for demographic variations in an African population, especially with regards to study settings and residence, as diabetes prevalence in urban areas is considered to be approximately double that in rural areas (Whiting et al., 2011). Over 55% of the selected studies were from urban, wealthy centres, and the model did not appropriately assign urban estimates to urban population, and rural estimates to rural population. As noted in preceding sections, this is a fact that can possibly affect other estimates reported in this thesis. Another factor that could have affected this estimate is that the case definition in respective studies could have been more inclusive. Additionally, the screening test for cases of diabetes in an individual study could have had a sub-optimal test-to-actual positives ratio (TAP ratio). According to Campbell and colleagues, the TAP ratio is a parameter or measure of potential bias in a disease frequency estimates that summarizes the properties of a diagnostic test and

true prevalence of a disease in a population (i.e. ratio of those who test positive to the screening test, to the actual number of people who have the disease in the population) (Campbell et al., 2008).

Study limitations

While the current study endeavoured to give population representative estimates of the prevalence of diabetes in Africa for the years 1990, 2000 and 2010, this however could have been limited by a number of factors.

For the pooled diabetes prevalence, I^2 was 97.9%. This also implies that there is very high heterogeneity across selected studies; and at $p<0.0001$, the heterogeneity is statistically significant. There is therefore strong evidence against the null hypothesis that studies are evaluating the same effect. For a combination of studies with such high heterogeneity, it may also not be appropriate to pool a summary effect. However, as reported earlier, there is very low research output in Africa, and the few studies have not been conducted under strict international guidelines, so heterogeneities can be expected. . In addition, restricting my analysis to studies that have the same study design, same sampling frame and same case definition is almost impossible.

Another important limitation is the inability to assess how closely representative these estimates were of the larger African population. Importantly, the prevalence from individual studies mainly reflect intrinsic characteristics specific to the study settings, and should not necessarily be viewed as representative of the region of country in which the study was conducted. The estimates should therefore be interpreted with caution. Moreover, despite the relatively high number of studies, data from many studies were incomplete. This affected my analysis, as results of potentially good studies, with clear sampling strategy and study designs, were not always detailed and therefore could not be explored further. In addition, some authors did not state clearly the diagnostic methods employed. Any of the diabetes criteria (earlier described in Methods) were ascribed to these studies if they were highly comparable. Age- and sex-specific prevalence could not, in detail, be reported, including corresponding prevalence on urban and rural settings, as these

were not always provided. As noted in the methods, single age (usually mean age) was mostly employed in the modelling. However, of the 45 studies selected, only 4 studies (8.9%) reported age-specific prevalence estimates that were employed in the modelling (Amoah et al., 2002, Duboz et al., 2012, Olatunbosun et al., 1998, Mbanya et al., 1997). This means that the estimated diabetes prevalence from the modelling may not well represent those of people from individual studies in the extreme age groups, i.e. very young and very old. This is a major limitation of this model. Determining the mean ages of study samples were also challenging. Some studies only gave the lower age limits, and in this case, the UN population estimates for that country and the year under review were employed to determine a possible age range. One important limitation of this study is the inability to separate the analysis for type 1 and type 2 diabetes respectively. Most studies were non-specific on the type of diabetes being reviewed. This could have given a clearer picture of type-specific diabetes in Africa, especially with confirmed reports of higher prevalence of type 2 diabetes in the continent (Motala et al., 2003).

However, in view of the increasing prevalence of diabetes with age in Africa, and relative association of type 2 with adults, we included studies conducted among people aged greater than or equal to 15 years in the final review and analysis. The estimates may therefore point to the burden of type 2 diabetes in Africa, for which previous studies have reported a higher prevalence in Africa. Additionally, the 48 selected studies spread across 28 countries in Africa with a total sample size of 102,517, and all extracted data from these studies have been included in the modelling (refer to **Table 3.17** and **Appendix 4**).

Public health response to diabetes in Africa

On the global scene, international organizations have responded well to diabetes control and its overall management in Africa, as this is clearly where the disease burden is growing fastest in the world (Unwin et al., 2001). In 2006, WHO and IDF jointly came up with recommendations aimed at addressing the rising burden of diabetes. Their main focus was on availability and pricing of insulin; they recommended equity pricing scheme for insulin for resource poor settings, and also encouraged twinning initiatives between high-income countries and LMIC towards achieving sustainable diabetes control projects (World Health Organization, 2006). The twinning initiative has been successful in some parts of Africa; Diabetes UK currently supports diabetes care in Mozambique, Norwegian Diabetes Association has been linked with successful diabetes control programmes in Zambia (Beran et al., 2010, Yudkin et al., 2009), and Novo Nordisk has also led many diabetes control initiatives in Africa (Mbanya and Ramiaya, 2006). There have also been some reports of support from non-governmental organizations (NGOs); International Insulin Federation and Diabetes Mali have helped establish sustainable programmes for insulin access and diabetes care in Mozambique, Zambia and Mali (Levitt, 2008, Silva-Matos and Beran, 2012b).

On this premise, many African governments have generally pointed to an appreciable increase in the management of diabetes in the continent. It is however clear, based on widespread hospital records, and results of epidemiological surveys, the statement was far too generalized and merely political, stating that a structured and organized health care system for diabetes in still lacking (Beaglehole, 2011, Mbanya and Ramiaya, 2006).

Challenges affecting diabetes control in Africa include poor financing, lack of awareness, inherent cultural beliefs, lack of trained health staffs, dearth of information on diabetes, poor data management system, and state of health systems, among others (Sobngwi et al., 2001). More donors and high political involvement have been advocated towards improving the financial strengths of resource-poor settings (Mbanya and Ramiaya, 2006). In many areas, due to high cost of oral

hypoglycemic drugs, many still cannot afford or do not have access to newer and more effective drugs (Idemyor, 2010).

A high discrepancy has been observed in health care access and diabetes management between rural and urban areas (Levitt, 2008). This has been linked to lack of awareness in many rural areas, especially on availability of facilities for detection and monitoring diabetes (Mbanya and Ramiaya, 2006). In fact, many still patronize alternate healing centres, due to inherent cultural beliefs, and patients often present back to standard health facilities at advanced stages of illness (Mbanya et al., 2006). In urban areas, many health centres cannot adequately screen and treat the complications of diabetes (Mbanya et al., 2006). Most health centres do not have endocrinologists, and when they are available, there are no facilities or well-equipped diabetic units to manage patients (Beran and Yudkin, 2006, Levitt, 2008). In many of these settings, most causes of diabetes deaths could have been preventable (Mbanya and Sobngwi, 2003).

Experts have reported that the hallmark for improvement in diabetes care and management in Africa lies in the development of favourable policy for diabetes at various country levels in Africa (Mbanya et al., 2006). Reports show that many African countries do not have a policy framework for diabetes control and this has affected the management and control of the disease in the continent (Beran and Yudkin, 2006).

This study has reported an increasing prevalence of diabetes in Africa, and this has presented a huge burden on individuals, society and government. The rapid rise in urbanization, population and life expectancies across the African continent, without any counter control measures has been hugely responsible for this increasing prevalence. It has been identified that information on diabetes epidemiology has increased; however, there is still dearth of data especially on chronic complications of diabetes (retinopathy, nephropathy and neuropathy). For example, Holmes and colleagues reported that, up till 2009, there were 84 population-based cross-sectional studies on diabetes in Africa, accounting for 7 studies per million people with diabetes in Africa, and this represent 8% of the total publications on diabetes in the

United States (Holmes et al., 2010). Therefore, more research on diabetes is still needed to adequately quantify the burden in the region. Largely, collaborations encompassing government, policymakers, diabetes associations, NGOs, donors and many stakeholders across several parts of the world may be effective in Africa. We hope the findings of this research can address these challenges, encourage more research and networks among experts, and help towards improved management and control of diabetes in Africa

4.3 CANCER

This study attempted to provide continent-wide pooled estimates of major cancers in Africa. Data employed were mainly from population based cancer registries. In the current study, I reported estimates of 12 major cancers in Africa (cervical, breast, prostate, ovary, oesophagus, bladder, Kaposi, liver, stomach, colorectal, lung and non-Hodgkin lymphoma). As data employed in the analysis were based on population based registries, the pooled estimates provided were based on a total population of about 33 million. This is the largest sample size from which estimates have been provided in this thesis.

The pooled estimate revealed that cervical cancer, breast cancer, Kaposi sarcoma, liver cancer and colorectal cancer were the top five cancers among women, while prostate cancer, Kaposi sarcoma, cancer of the oesophagus, liver cancer and lungs cancer were the top five cancers among men (**Table 4.3**). These orders of top cancers reported in this study are similar to those reported by the GLOBOCAN studies. For example, in 2002, GLOBOCAN reported that the top cancers among women in Africa were cervix, breast, liver, stomach and Kaposi; and among men, prostate, liver, Kaposi, stomach and lungs (Parkin et al., 2005, Parkin et al., 2008). The 2008 GLOBOCAN study did not specify the incidence rates of Kaposi sarcoma among men and women, however, the top five cancers among women in Africa were cervix, breast, liver, colorectal and non-Hodgkin, and among men, prostate, liver, lungs, colorectal and oesophagus (Ferlay et al., 2010, Jemal et al., 2011) (**Table 4.3**). While these GLOBOCAN studies have provided estimates on major cancer types in Africa over the years, there are still concerns if their modelling truly reflects the burden of cancers in the African population. Some of their limitations include non-availability of incidence and mortality data from certain parts of Africa. Estimates provided were said to be based on large data sets which have been modelled to account for incidence and mortality rates by age, country and year. Sources of these datasets are said to be from cancer registries' data submitted to the International Agency for Research on Cancer (IARC) and the International Association of Cancer Registries

(IACR). As noted earlier in my methods, these data are not readily available and could not afford me further opportunity for direct comparisons. Besides, other details on the statistical analysis and modelling are not usually provided. This point to the general observation in the introduction that there is little or no reliable data to work with in Africa and that most global models (like the GLOBOCAN) are based on data from other non-African countries (in this case, the large data set) inputted into African countries.

Meanwhile, according to the 2010 IHME GBD estimates, the top five cancers contributing to global DALYs and deaths were lungs, liver, stomach, colorectal and breast (**Table 4.4**). It may be inappropriate to make direct comparisons with these estimates as they are global estimates and may not necessarily be applicable specifically to the African region.

Table 4.3. Summary of cancer incidence rates (per 100,000 person years) among men and women from selected published reports

Site	*1990 (Parkin et al., 1999)*		*2000* (Parkin et al., 2001a)*		*2002 (Parkin et al., 2005, Parkin et al., 2008)*		*2008 (Ferlay et al., 2010, Jemal et al., 2011)*		*2014 Current study (95% CI)*	
	M	F	M	F	M	F	M	F	M	F
All	-	-	81.2-217.5	94.1-176.4	99.0-213.7	85.2-163.2	88.1-235.9	96.7-161.1	-	-
Kaposi	-	-	-	-	12.3	4.6	-	-	14.3 (11.9, 16.7)	6.5 (5.2, 7.8)
Liver	2.6-16.8ł	1.5-9.4	14.8	6.7	14.8	6.2	11.6	5.3	12.6 (10.0, 15.3)	5.7 (4.4, 7.0)
Colorectal	1.2-6.6	1.5-9.4	5.7	4.6	5.4	4.2	6.9	5.0	5.3 (4.0, 6.5)	3.9 (2.9, 4.9)
Stomach	3.4-10.3	1.7-9.0	8.1	6.5	6.2	4.9	4.7	3.3	5.6 (4.2, 7.1)	3.8 (2.9, 4.7)
Lung	1.2-18.1	0.5-5.6	4.9	1.8	2.4-23.1	0.6-6.9	8.4	2.7	9.3 (6.8, 11.7)	1.9 (1.3, 2.5)
NHL	3.2-7.2	2.5-5.4	6.8	4.5	5.6	3.9	6.3	4.1	3.9 (2.8, 5.0)	2.9 (2.1, 3.7)
Oesophagus	1.0-21.6		6.2		7.8		6.7		13.4 (10.2, 16.6)	
Bladder	1.4-13.8		-		4.5		6.7		5.8 (4.2, 7.4)	
Cervix	7.3-30.4		31		29.3		28.0		28.2 (22.1, 34.4)	
Breast	8.6-22.8		22		23.4		25.2		17.7 (13.0, 22.4)	
Ovary	2.0-4.7		-		4.3		4.2		3.6 (2.7, 4.4)	
Prostate	2.6-16.9		19.8		16.0		17.5		14.5 (10.9, 18.0)	

**sub-Saharan Africa, ł range values given*

Table 4.4. Global and Sub-Saharan African DALYs and deaths from major cancers

CANCERS	*GLOBAL*				*SUB-SAHARAN AFRICA*			
	DALYs (millions)		*DEATHS (millions)*		*DALYs (thousands)*		*DEATHS (thousands)*	
	1990	*2010*	*1990*	*2010*	*1990*	*2010*	*1990*	*2010*
All sites	148.1	188.5	5.8	8.0	7406.5	11033.0	231.2	352.0
Oesophagus	8.1	8.9	0.34	0.4	498.8	620.3	18.7	24.3
Stomach	18.5	16.4	0.77	0.75	512.2	622.4	18.9	24.1
Liver	13.2	19.1	0.46	0.75	1047.7	1395.1	32.4	45.0
Lung	23.9	32.4	1.03	1.53	378.3	521.1	14.3	20.1
Breast	8.8	12.0	0.32	0.44	358.6	727.3	11.5	23.3
Cervix	5.6	6.4	0.19	0.23	1040.8	1387.1	33.0	45.0
Ovary	3.0	4.1	0.11	0.16	93.7	167.8	3.0	5.4
Prostate	2.4	3.8	0.16	0.26	100.2	219.7	5.6	12.3
Colorectal	10.6	14.4	0.49	0.71	257.8	483.7	9.4	17.7
Bladder	2.4	3.0	0.12	0.17	96.7	125.6	3.8	5.0
NHL	4.5	5.9	0.14	0.21	444.1	694.0	9.3	15.3

Source: (Lozano et al., 2012, Murray et al., 2012)

4.3.1 Observations relevant to some specific types of cancers in Africa

In the current study however, the pooled incidence rate for cervical cancer was 28.2 per 100,000py, which was also the highest cancer incidence reported. This is comparable with the 2002 and 2008 GLOBOCAN estimates for Africa at 29.3 and 28.0 per 100,000py respectively, which were also the highest incidence rates reported by the respective studies (Ferlay et al., 2010, Parkin et al., 2005), further underpinning the high burden in the continent (**Table 4.3**). This is further supported by previous reports, in which cervical cancer is rated the second leading cancer among women, but however the most common cancer in Africa and many low- and middle-income countries (Ferlay et al., 2010, Parkin et al., 2008). In a related study, Forouzanfar and colleagues reported that the cumulative probability of incidence of cervical cancer between 1980 and 2010 was highest in sub-Saharan Africa, ranging from 2.7 in West to 4.1 in Central Africa, respectively (Forouzanfar et al., 2011). Having been established that almost all cervical cancer cases result from human papilloma virus (HPV) infection (Ferlay et al., 2010, Parkin et al., 2005), it is believed that the low coverage of HPV vaccine, low cost cervical screening and other interventions targeted at HPV may have, in most instances, led to the relatively high burden of cervical cancer in the region (Forouzanfar et al., 2011). For example, according to the WHO, HPV vaccine was only introduced in 41 countries globally in 2012, and there was no detail of an African country that is fully involved in this immunization scheme (World Health Organization, 2014c). However, in a recent review in sub-Saharan Africa, only six countries were identified to have met the GAVI Alliance requirements for supporting the introduction of HPV vaccine (Perlman et al., 2014). Meanwhile, according to the 2010 IHME GBD estimates, there were about 6.4 million DALYs and 230 thousand deaths from cervical cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). This is not based on the African population; therefore their estimates cannot be compared to the current study. In sub-Saharan Africa however, IHME estimated that DALYs from cervical cancer increased from 1 million in 1990 to 1.4 million in 2010 (40% increase), while

deaths increased by 36.4% from 33,000 to 45,000 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

Previous reports have shown that breast cancer is the leading cancer among women and second most common cancer globally (Jemal et al., 2011). It also has the highest survival rates due to improved medication and treatment response (Soerjomataram et al., 2012, Coleman et al., 2008). According to the 2010 IHME GBD estimates, there were about 12 million DALYs and 440 thousand deaths from breast cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). Again, this cannot be compared to the current estimates in this study, as they broadly based on the total world population. In sub-Saharan Africa however, IHME estimated that DALYs from breast cancer increased from 358,600 in 1990 to 727,300 in 2010 (over 100% increase), while deaths also increased by over 100% from 11,500 to 23,300 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012). The pooled estimate from this study was 17.7 per 100,000py. This is also the second highest incidence rate reported in this study, but however remarkably lower than the GLOBOCAN 2002 and 2008 estimates at 23.4 and 25.2 per 100,000py respectively (**Table 4.3**). The relatively lower estimate reported in this study in comparison to previous reports may be because this is not an age-standardized statistical synthesis and in fact does not include any further modelling and consideration of population demographics. However, higher breast cancer incidence rates generally in most parts of Africa may be due to higher prevalence of obesity, estrogen exposures, smoking, and fats consumption, which is peculiar among urban African dwellers. In this study, we could not explore this further as most studies did not provide incidence rates separately for urban and rural dwellers. Meanwhile, Forouzanfar and colleagues further reported that the cumulative probability of incidence of breast cancer between 1980 and 2010 was second highest in sub-Saharan Africa, ranging from 2.9 in Central and West to 5.6 in Southern Africa, respectively (Forouzanfar et al., 2011).

There has been a gradual increase in the incidence of prostate cancer in Africa in the last two decades. In 1990, incidence rates of prostate cancer were between 2.6 and

16.9 per 100,000 across the main African regions in 1990 (Center et al., 2012, Pisani et al., 1999). In 2007, reports show that prostate cancer incidence rates rate ranges from 4.7-19.8 per 100,000py in West Africa to 10.7-38.1 per 100,000py in East Africa (Chu et al., 2011). GLOBOCAN estimated an incidence rate of 16.0 per 100,000 accounting for 10.6% of all male cancers in 2002 (Parkin et al., 2005), and an incidence of 17.5 per 100,000py accounting for over 12% of male cancers in 2008 (Ferlay et al., 2010). From this study, the estimated incidence rate was 14.5 per 100,000py. The relatively lower estimate reported may still reflect the lack of detailed modelling and a consideration of age and rapidly population demographics in Africa. Meanwhile, according to the 2010 IHME GBD estimates, there were about 3.8 million DALYs and 260 thousand deaths from prostate cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from prostate cancer increased from 100,200 in 1990 to 219,700 in 2010 (over 100% increase), while deaths also increased by over 100% from 5,600 to 12,300 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

The high prevalence of HIV/AIDs in Africa is the single most important factor for an increase in HIV-associated cancers, mainly Kaposi sarcoma caused by Kaposi's sarcoma-associated herpes virus (KSHV) (Feller et al., 2010, Mosam et al., 2009). Many studies have reported interactions between HIV/AIDS and many NCDs, especially cancers (UNAIDS, 2011). According to Byass and colleagues, the mortality rates of many NCDs are relatively higher among HIV positives compared to negatives. For cancers, oral neoplasms had the highest mortality rate ratio at 19.2, followed by reproductive neoplasms (female) 14.3, digestive neoplasms 13.0, breast neoplasms (female) 9.6, respiratory neoplasms 6.0 and other unspecified neoplasms 7.7(Byass et al., 2013a). It is believed that a better understanding of this interaction, while drawing from the HIV control experience, may help in instituting appropriate response to the growing burden of NCDs in Africa. Further details on HIV and NCDs are in **Section 1.1.4** and **Table 1.3**.

Meanwhile, in this study, the incidence rates of Kaposi sarcoma were 14.3 and 6.5 per 100,000 among men and women respectively, which is higher than the incidence rate reported in the 2002 GLOBOCAN (12.3 and 4.6 per 100,000) (**Table 4.3**) (Parkin et al., 2005). The current estimate shows that Kaposi sarcoma is rated the second commonest cancer among men (after prostate cancer at 14.5 per 100,000py), and third commonest cancer among women (after cervical and breast cancers at 28.2 and 17.7 per 100,000py, respectively). This is almost in line with previous reports, in which Kaposi sarcoma is rated the most common cancer among men and second most common cancer among women (Parkin et al., 2008). Meanwhile, in Eastern and Southern Africa, with higher prevalence rates of HIV/AIDS, Kaposi sarcoma is the most commonly diagnosed cancer with incidence rate 20 times as high as in other parts of Africa (Parkin et al., 2008, Chokunonga et al., 1999).

Cancer of the oesophagus is a leading cause of cancer among southern and eastern African men, with incidence rates seven times higher than observed in central, northern and western Africa (Parkin et al., 2008, Madebo et al., 1994, Sumeruk et al., 1992). In Africa, a geographical predisposition has been thought to be responsible for the high incidence especially in Kenya and the Eastern Cape province in South Africa where a remarkably high incidence (76.6/100,000py) was recorded among men in the 1990s (Parkin et al., 2008, Parkin et al., 2003). The pooled estimate from this study is 13.4 per 100,000 among men, which is relatively higher than the 2002 and 2008 GLOBOCAN estimates at 7.8 and 6.7 per 100,000py, respectively (**Table 4.3**) (Ferlay et al., 2010, Parkin et al., 2005). This may be indicative of a gradually increasing burden of oesophageal cancers among men in these sub-regions. Reports show that increased smoking, harmful use of alcohol, HPV infection, poor consumption of fruits and vegetables, consumption of foods contaminated with *Fusarium verticillioides,* a filamentous fungus that produces carcinogenic mycotoxin *fumonisin B2* are indicative (Hendricks and Parker, 2002). Meanwhile, according to the 2010 IHME GBD estimates, there were about 8.9 million DALYs and 400 thousand deaths from oesophageal cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from oesophageal cancer increased from 498,800 in 1990 to 620,300 in 2010 (24.4%

increase), while deaths increased by 30% from 18,700 to 24,300 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

Liver cancer is rated among the leading causes of cancers in Africa due to its infective aetiology and association with aflatoxin B1, which are relatively more prevalent in Africa (Parkin et al., 2003). The pooled estimate from this study was 12.6 and 5.7 per 100,000py among men and women, respectively. This is quite comparable with the GLOBOCAN 2002 and 2008 estimates at 14.8 and 11.6 per 100,000 among men, and 6.2 and 5.3 per 100,000py among women, respectively (Ferlay et al., 2010, Parkin et al., 2005) (**Table 4.3**). As noted above, the high incidence of liver cancer in Africa reported is believed to be due to chronic infections from hepatitis B virus (HBV) and hepatitis C virus (HCV) in most parts of Africa, where it is rated the most common cancer, constituting about 25% of all cancers in men and women (Mbakop et al., 1992, Parkin, 1994). Available evidence shows that interventions addressing these chronic viral infections in Africa are poor (Burnett et al., 2011).

According to the WHO, the global coverage of Hepatitis B vaccine was about 79%, covering 181 countries in 2012, following its recommended introduction into routine immunization schedules of all endemic countries in 1992 (World Health Organization, 2014c). However, an estimated 22.6 million infants are still missing out on three doses of the vaccine, with most of these residing in Africa (World Health Organization, 2014c). Hepatitis B vaccine is now also among the routine infant immunization programmes in some African countries (Burnett et al., 2011). The vaccine is given in two or three serial doses, usually introduced at 6 weeks or 3 months, and repeat doses given at 6 months and 9 months, depending on the national immunization programme of each country (Burnett et al., 2011). Studies have shown that Hepatitis B vaccination may provide long term protection in more than 90% of healthy people (Shepard et al., 2006). However, some studies have stated that vaccine-induced immunity acquired at this early life, as measured by anti-HB levels, may have declined around ages 30-40 years and above, especially among vaccinees

who are immunocompromised (Shepard et al., 2006). As such, when babies who received Hepatitis B vaccine attain this age group (≥30 years), they may be susceptible to HBV if booster dozes of the vaccine are not given. Follow-up studies have further confirmed that most vaccinees (at 10 or more years post-vaccination) may develop a rapid rise in anti-HB when booster dozes of Hepatitis B vaccine are given (Shepard et al., 2006). Moreover, another important factor is that most of today's global adults were born before Hepatitis B vaccine was introduced and implemented (Byass, 2014). Thus, an effective intervention, which gives hope for a reduction in liver disease in the near future, is to administer booster doses of Hepatitis B vaccine to all adults (Byass, 2014). As well as boosting immunity of those who have been vaccinated, this can also ensure some adults are given their first doses of the vaccines. However, a South African study suggested that the proportion of an adult population in an African setting that is fully vaccinated may be low, as the coverage among health care workers, which should be presumably high, was only 19.9% (Burnett et al., 2011). Based on the 2010 IHME GBD estimates, there were about 19.1 million DALYs and 752 thousand deaths from liver cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from liver cancer due to hepatitis B infection increased from 491,400 in 1990 to 656,100 in 2010 (33.5% increase), while deaths increased by 38.8% from 15,200 to 21,100 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

High prevalence of *Schistosoma Haematobium* parasite (which causes bladder infection- Schistosomiasis) is thought to be the link to the relatively higher incidence of bladder cancer among men in Africa, especially in resource-poor riverine communities (Fedewa et al., 2009). The highest incidence and mortality globally was reported in Northern Africa, especially in Egypt with an incidence rate of about 37.1/100,000py in the 2000s (Heyns and van der Merwe, 2008). Some western African countries (Mali and Niger) also have higher incidences compared to other parts of Africa (Heyns and van der Merwe, 2008). This study reported an estimate of 5.8 per 100,000py among men, which is fairly comparable with the GLOBOCAN 2002 and 2008 estimates at 4.5 and 6.7 per 100,000py, respectively (Ferlay et al.,

2010, Parkin et al., 2005) (**Table 4.3**). From the 2010 IHME GBD estimates, there were about 3.0 million DALYs and 170 thousand deaths from bladder cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from bladder cancer increased from 96,700 in 1990 to 125,600 in 2010 (30% increase), while deaths increased by 31.6% from 3,800 to 5,000 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

In the 1990 GLOBOCAN study, the incidence rate of ovarian cancer ranged between 2.0 and 4.7 per 100,000py across the main African regions (Parkin et al., 2003, Parkin et al., 1999). In 2002 and 2008, GLOBOCAN reported incidence rates of 4.3 and 4.2 per 100,000py in Africa, respectively (**Table 4.3**) (Ferlay et al., 2010, Parkin et al., 2005). In this study, the estimated ovarian cancer incidence rate was comparable with previous reports at 3.6 per 100,000py. According to the 2010 IHME GBD estimates, there were about 4.1 million DALYs and 160 thousand deaths from ovarian cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). For reasons already noted above, this can still not be compared to the African population. In sub-Saharan Africa however, IHME estimated that DALYs from ovarian cancer increased from 93,700 in 1990 to 167,800 in 2010 (79.1% increase), while deaths increased by 80% from 3,000 to 5,400 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012). Meanwhile, some studies have shown racial differences in the risk of ovarian cancer, with risk lower among women of African descent than observed among white women (Ness et al., 2000). This may be partly responsible for the lower incidence rate reported in this study.

As noted in the introduction, lung cancer is rated the most common cancer globally (Ferlay et al., 2010). In this study, a high incidence rate was estimated among men (9.3 per 100,000py) compared to a very low rate among women (1.9 per 100,000py). This estimate is comparable with the 2008 GLOBOCAN estimate at 8.4 and 2.7 per 100,000py among men and women respectively (Ferlay et al., 2010) (**Table 4.3**). Generally, the prevalence of lung cancer is lower in many African countries (Ferlay et al., 2010). When compared to global estimates of cancers, the lower incidence

rate in Africa may be due to relatively lower smoking rates and lesser exposures to industrial and environmental pollution than some other parts of the world (Fadahun et al., 2011). The gender difference noted above may still reflect the reported higher smoking rates among men compared to women in the Africa region (Jha et al., 2002). Meanwhile, according to the 2010 IHME GBD estimates, there were about 32.4 million DALYs and 1.53 million deaths from lung cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from lung cancer increased from 378,300 in 1990 to 529,100 in 2010 (40% increase), while deaths increased by 41% from 14,300 to 20,100 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

Colorectal cancer is also increasing in Africa (Dakubo et al., 2010). In this study, the pooled estimates of colorectal cancer among men and women were 5.3 and 3.9 per 100,000py, respectively. This is comparable with the 2002 and 2008 GLOBOCAN estimates of colorectal cancers at 5.4 and 6.9 per 100,000py among men, and 4.2 and 5.0 per 100,000py among women, respectively (Ferlay et al., 2010, Parkin et al., 2005) (**Table 4.3**). A 2012 study on sub-Saharan Africa reported an incidence rate of 4.38 and 3.69 per 100,000py among men and women, respectively (Graham et al., 2012), which is also comparable with the current estimate. The increasing incidence of colorectal cancer in Africa has been linked to a gradual adoption of urban diets with high fats and cholesterol content, and a low consumption of fruits, vegetables and whole grains (Dakubo et al., 2010). However, in the 2010 IHME GBD estimates, there were about 14.4 million DALYs and 710 thousand deaths from colorectal cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from colorectal increased from 257,800 in 1990 to 483,700 in 2010 (87.6% increase), while deaths increased by 88.3% from 9,400 to 17,700 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

Many studies have reported that the incidence of stomach cancer is high in Africa (Ghoshal et al., 2010). From this study, the estimated incidence rates were 5.6 and

3.8 per 100,000 among men and women, respectively. This is comparable with the 2002 and 2008 GLOBOCAN estimates of stomach cancers at 6.2 and 4.7 per 100,000 among men, and 4.9 and 3.3 among women, respectively (Ferlay et al., 2010, Parkin et al., 2005) (**Table 4.3**). The relatively high incidence rate may be due to presence of *Helicobacter Pylori* infection in many parts of Africa, which is indicated in most cases of peptic ulcer disease (Ghoshal et al., 2010). In fact, in some Southern African regions, the incidence of stomach cancer has been reported to be as high as 98/100,000 due to mix of several population groups and races (Segal et al., 2001). From the 2010 IHME GBD estimates, there were about 16.4 million DALYs and 755 thousand deaths from stomach cancer worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from stomach cancer increased from 512,200 in 1990 to 622,400 in 2010 (21.5% increase), while deaths increased by 27.5% from 18,900 to 24,100 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

Previous reports have shown that non-Hodgkin lymphoma is rare in Africa with incidence rates relatively lower compared to those of European and North American countries (Sissolak et al., 2010). From this study, incidence rates of 3.9 and 2.9 per 100,000 were estimated among men and women, respectively. This is lower compared with the 2002 and 2008 GLOBOCAN estimates of stomach cancers at 5.6 and 6.3 per 100,000 among men, and 3.9 and 4.1 among women, respectively (Ferlay et al., 2010, Parkin et al., 2005) (**Table 4.3**). These lower figures, as explained earlier, may further underscore the lack of detailed statistical synthesis and non-consideration of the age-specific incidence rates (including those of childhood cancer, which has high incidence rates of Burkitt's lymphoma) and rapidly evolving population structure in Africa. Available evidence suggests that Burkitt's lymphoma, a variant of NHL and monoclonal B-cell lymphoma, which accounts for about 25-50% of childhood cancers in eastern, southern and western African regions, may be responsible for an increasing trend in the incidence of NHL (Lewis et al., 2012). This has been linked to an infection with the Epstein Barr Virus (EBV), which causes the oncogenic feature (deregulation of the C-MYC oncogene) responsible for the

lymphoma (Lewis et al., 2012). Global studies rated NHL as the fifth commonest cancer in Africa, this is still subject to more detailed disease burden estimation (Ferlay et al., 2010). According to the 2010 IHME GBD estimates, there were about 5.9 million DALYs and 210 thousand deaths from NHL worldwide in 2010 (Lozano et al., 2012, Murray et al., 2012). In sub-Saharan Africa however, IHME estimated that DALYs from NHL increased from 444,000 in 1990 to 694,000 in 2010 (56.3% increase), while deaths increased by 64.5% from 9,300 to 15,300 over the same period, respectively (see **Table 4.4** for details) (Murray et al., 2012, Lozano et al., 2012).

Study limitations

Generally, this study attempted to provide sex-specific incidence rates of leading cancers in Africa, and comparing these with reported global estimates, towards appreciating the variations in reported estimates, and informing various stakeholders on the problems arising from lack of detailed cancer registration in Africa. However, this study could have been constrained by a number of factors. While the retained studies spread across various parts of Africa, only 27 population-based registries were represented. Most of these cancer registries are restricted to specific locations in the respective countries, and do not all cover national populations. It is therefore difficult to say that the registry reports were representative of the total population of the country where the registry is based. In addition, this study mainly included very few registries from rural areas where more people generally reside in Africa and they typically reported lower cancer incidence rates, compared to the urban registries that reported higher incidence rates; this may thus potentially affects our estimates with an under-estimation of cancer burden in rural areas and an over-estimation in urban areas. Moreover, not all studies reported basis of cancer diagnosis, it was therefore based on evidences of epidemiological rigours and clinical case ascertainment (active/ passive case finding) that some studies were included. Another limitation, which actually resulted in the lack of modelling and estimation of number of specific cancer cases, was that many studies only gave overall crude incidence rates, and did not report any age-specific incidence rates.

For all the pooled cancer prevalence rates, I^2 ranged between 89.0-99.1%. This implies that there is very high heterogeneity across selected studies; and at $p<0.0001$, the heterogeneity is statistically significant. There is therefore strong evidence against the null hypothesis that studies are evaluating the same effect. For a combination of studies with such high heterogeneity, it may also not be appropriate to pool a summary effect. However, as reported earlier, there is very low research output in Africa, and the few studies have not been conducted under strict international guidelines, so heterogeneities can be expected. In addition, restricting my analysis to studies that have the same study design, same sampling frame and same case definition is almost impossible. Lastly, I cannot say with all certainty how closely representative these estimates were of the larger African population. However, this study provides ample evidence on the need for more detailed cancer data collation and registration across many African settings towards ensuring a true burden of cancer is reflected.

Public Health response to Cancer in Africa

i. Perceptions on cancers in Africa

Perceptions on cancers among Africans are affected by a wide range of socio-cultural behaviours, including inherent beliefs and norms (Parkin, 1994).

Healthcare-seeking behaviour: A survey in Lagos, Nigeria, showed that 81.7% of cervical cancer patients had never heard of the disease prior to diagnosis, 98% believed that the cancer was not serious and could be cured, 50% thought the symptoms were due to irregular menses or a sexually transmitted infection, while only 9% knew the disease was cervical cancer and could have bad prognosis (Anorlu, 2008). Moreover, many African women with cervical and breast cancers present late to health facilities because their husbands have not allowed them to do so early enough (Anorlu, 2008). This further highlights the gender inequity plaguing many indigenous African communities (Parkin et al., 2008). It is also important to note that some inherent traditional practices have put many African women at risk of cancers, as early marriage and high parity are quite predominant (Sitas et al., 2008).

Health service delivery: The behavioural challenge facing the delivery of health services may also be related to stigmatization and discrimination (Lingwood et al., 2008). Many a time, in the course of receiving care and treatment, cancer patients in Africa have been subjected to varying degrees of stigmatization, especially from health workers (Sitas et al., 2008), and this further reduces the patronage of standard health services. In fact, when care is finally sought, many of these cancer patients prefer to be taken to traditional healers, where they believe their illnesses are kept secret and the services rendered are thought to be comparatively cheaper. They only present to standard health facilities when the cancer is just too advanced for any curative treatment (Sitas et al., 2008)

ii. Challenges affecting established architecture for cancer care in Africa

Governance and Policies: As noted above, tobacco smoking is increasing in many African countries due to lack of regulatory policies on its sales and use (Otañez et al., 2009). In fact, due to the support many tobacco companies give to African governments, they have been able to manoeuvre policymakers in favour of tobacco sales and use (Saloojee and Dagli, 2000, Otañez et al., 2009). Experts have clamoured for better public awareness on the need for increased taxation on tobacco products, with money derived diverted into useful health promotion measures (Groenewald et al., 2007b). In addition, many African countries do not offer patient-friendly policies related to taxes on cancer medications and screening technology, and as such, some chemotherapy drugs have been found to cost about 1000% more than the costs in United Kingdom and other parts of Europe (Lingwood et al., 2008). Due to this high taxation and the associated high cost of cancer treatment, the African Organization for Research and Training in Cancer (AORTIC) is now fronting continent-wide lobbying to convince African governments to cut taxes on drugs, including those on medical equipment (African Organization for Research and Training in Cancer, 2013).

Health programmes and service delivery: Recent studies show that some African countries are beginning to step-up efforts to address cancers by convening awareness campaigns programmes on cancers and its risk factors (Sitas et al., 2008). In addition, screening programmes for cervical cancer, breast cancer and Burkitt's lymphoma have been established in some countries (Morris, 2003, Albrecht, 2011). However, the major challenge lies in the sustainability, as ongoing programmes have been aborted abruptly in many cases (Lingwood et al., 2008). Palliative care programmes do exist in some settings, but not well equipped to offer pain relieving medications and overall well-being of cancer patient (Jemal et al., 2012, Harding et al., 2013, Grant et al., 2011). Cancer treatment is gradually improving in Africa, but cancer screening and detection, especially in rural areas still remain an important public health issue (Kingham et al., 2013). The Oxford Declaration calls for African governments to work with international partners and NGOs to implement effective

cancer screening programmes using appropriate medical technology (Oxford Declaration, 2009).

Training and health workforce: Training programmes specific for cancer management are rare in Africa (African Organization for Research and Training in Cancer, 2013, Adebamowo and Akarolo-Anthony, 2009). This is one of the major challenges that has resulted in the high mortalities from cancers in Africa, as many medical practitioners do not have the requisite expertise to manage cancers, especially in rural Africa (Jemal et al., 2012). As highlighted above, health workers are still not enough to meet the increasing demand from many diseases, including cancers, in Africa (Parkin et al., 2008). Reports show that only 3% of the world health workers currently live and work in sub-Saharan Africa (de-Graft Aikins et al., 2010a). In recent times, there has been an increase influx of medical practitioners to high income countries due to poor welfare and condition of services (Mungal-Singh, 2011).

Health system funding: Generally, the health care systems of many African countries are poorly equipped, despite accounting for a greater fraction of the global cancer burden (Lingwood et al., 2008). From the 2009 Oxford Declaration, it was clearly evident that many African governments do not recognize the growing cancer epidemics in the continent, and as such many health systems have not been adequately equipped to address this (Oxford Declaration, 2009). Budget allocation for cancers by many African governments is low, as this is rarely considered a priority due to the high burden from HIV/AIDS, tuberculosis and malaria (Boyle et al., 2008). In the wake of cost-effective measures for cancer control, including vaccination against infectious causes, donor funding (from international organizations and non-governmental organizations) for cancer control has been greatly advocated (Adebamowo and Akarolo-Anthony, 2009).

iii. Opportunities for improvement

Lingwood et al. noted that to establish a comprehensive cancer care programme in Africa, an integrated effort of clinicians, oncologists, epidemiologists and public health experts within an effective health system is paramount, as these are opportunities that can prompt effective control, detection and management of cancer in the region (Lingwood et al., 2008). These are discussed further under this section.

Screening, Diagnosis and Treatment: The WHO has championed the screening and early detection of cancers globally, especially in developing countries where the burden of cancers is highest (World Health Organization, 2013a). Research findings show that one third of cancers are preventable and/ or treatable in developing countries if detected early, thus making the presence of an effective screening and diagnosis system across countries a vital component in cancer management (Cazap, 2012). However, this is rarely the case in Africa, as resources are far too limited to be diverted to cancer diagnosis in the face of other health challenges (Parkin et al., 2008). For example, Albrecht reported lack of cancer screening programmes in Africa, citing that 80% of South African women have never had a pap smear, which is a reflection of the lack of a national cytology plan in many African countries (Albrecht, 2011, Cronjé and Beyer, 2007). Cronje et al reported that in some African countries, minimal screening infrastructure does exist (Cronjé and Beyer, 2007); however, due to lack of trained health staff, active cancer screening has been poor and even decreasing in some settings (Lingwood et al., 2008).

Generally, cancer management involve any or a combination of chemotherapy, surgery and radiotherapy (Kingham et al., 2013). Chemotherapy has been proven to be effective in treating many cancers, usually indicated for cancers that have spread to other body parts (Cazap, 2012). However, its use in Africa is subject to availability and the ability of patients to pay (Kingham et al., 2013). Reports show that only 5% of cancer patients undergo chemotherapy in Africa (Lingwood et al., 2008). Surgery is indicated for cancers at early stages, as the tumour is usually localized and easy to remove, with chemotherapy or radiotherapy mainly serving as adjuvant therapies

(Kingham et al., 2013). The challenge in many African settings is that many medical practitioners lack the expertise to perform surgeries, thus post-surgery prognosis is usually poor (Lingwood et al., 2008). There is also challenge from lack of effective analgesics and follow-up after surgery (*discussed further under palliative care*) (Boyle et al., 2008, O'Brien et al., 2013). In sub-Saharan Africa, radiotherapy has been shown to improve surgical outcomes for cancers including breast and colorectal cancer (Barton et al., 2006). However, oncologist have reported that the use of radiotherapy is limited owing to lack of adequate medical infrastructure, specialty centres, radiologists and technical expertise in many African regions (Boyle et al., 2008). In 2013, research findings show that only 23 countries in Africa offer radiotherapy, with external beam radiotherapy the most widely used (Abdel-Wahab et al., 2013). Other types of radiotherapy that are rarely used in Africa include brachytherapy, which is highly indicated for cervical cancers (Kingham et al., 2013).

Most advancement in cancer treatments in Africa have been based on new and effective vaccines (Boyle et al., 2008). As noted earlier, the coverage of HBV vaccine among infants in Africa is increasing, but current reports show that the percentage of adult population that is fully vaccinated may be low (World Health Organization, 2014c). For HPV vaccine, the coverage is generally low with only 6 countries in Africa currently identified to have met the GAVI Alliance requirements for supporting the introduction of HPV vaccine (Perlman et al., 2014). Vaccinations are important in the management of cancers in Africa due to the high prevalence of cancers with infectious aetiologies (Parkin, 2006b). Assessing current vaccination programmes, monitoring vaccine effectiveness, and ensuring sustainable and affordable vaccination with active community participation are believed to be vital to successful treatment of cancers (Kingham et al., 2013).

Palliative care: Palliative care has attracted lots of interest globally and has been adjudged by the WHO as an important component of the cancer care pathway (Morris, 2003, Harding et al., 2013, World Health Assembly, 2005). Research findings have shown that about 80% of cancer cases are detected late in Africa (Wakabi, 2007); hence chemotherapy, radiotherapy and surgical treatments may not

really suffice. Thus, towards ensuring an improved management of cancer, particularly in Africa, palliative care is imperative and is now believed to be a practical and humane solution to Africa's cancer burden (Wakabi, 2007, Harding et al., 2013, Stjernswärd et al., 2007). Some palliative care initiatives have been created across Africa, including the African Palliative Care Association (APCA), which works with many African health care providers to relieve the pains and improve overall wellbeing of people at advanced stages of cancers and other terminal illnesses (O'Brien et al., 2013, Harding et al., 2013); however, reports have shown that these initiatives have been limited by the unavailability and unaffordability of effective pain-relieving medications (O'Brien et al., 2013). According to a 2004 survey, only five African countries have cancer palliative care programmes and/ or allow the dispensing of oral morphine (Harding et al., 2013, Wright et al., 2008), with this increasing to 28 out 57 African countries in 2010 (Grant et al., 2011). It was further observed that with strong political will, increased funding, capacity building and establishment of improved treatment facilities, sustainable palliative care programmes may be established in Africa (Grant et al., 2011), as this was the case in Uganda, which is presumably the only country in the world where nurses are allowed to prescribe morphine (Morris, 2003).

Research and technical training: Experts have clamoured for more rigorous research that will inform better care of cancer patients in Africa (Morhason-Bello et al., 2013). A bottom-up approach is thought to be helpful especially from detailed vital statistics and cancer registration at rural hospital levels, which can then be synergized with larger population-based cancer registries in urban centres (Parkin, 2006a). With this, appropriate estimation of the burden can be expected, which can then help in policy planning and practices for cancer management in Africa. Importantly, studies can be more effective if they tackle problems that address native health needs, which can be transferable to other comparable health systems in Africa (Adebamowo and Akarolo-Anthony, 2009). Improved technology should be advocated for, especially for cancer detection and screening, standard radiotherapy machines and other related medical equipment. Finally, health workers should adequately familiarize themselves

with technological advancements in cancer management, and the training of health workers on current management of cancer patients and/ or based on disseminated research findings should be greatly encouraged.

Cancer registration: According to Parkin et al., incidence data on cancers are better sourced jointly from hospital-based and population-based cancer registries, as this will allow new cancer cases to be sourced from within hospitals and outwit hospital (Parkin, 2006a). According to the WHO, many African countries still do not have a functional cancer registration system (World Health Organization, 2013a). The few cancer registries in these regions only cover the urban cities and do not really spread to the rural areas (Awadelkarim et al., 2010). In fact, only 5 cancer registries from 5 African countries contributed to the first volume of "Cancer Incidence in Five Continents" (Whelan and Ferlay, 1992, Valsecchi and Steliarova-Foucher, 2008). It is estimated that in 1990, only 5% of African countries were covered by functional cancer registries, with this increasing to about 20% in 2008 (Ferlay et al., 2010). The WHO further reported that cancer registration globally has progressed haphazardly over the last two decades as most countries do not have an official policy to support cancer registration (World Health Organization, 2013a). Moreover, resource allocation for cancer registration is low in many developing countries as this is perceived a luxury amidst other challenging health issues (Valsecchi and Steliarova-Foucher, 2008).

Meanwhile, vital registration systems are also important sources of mortality data on cancers (Parkin, 2001). In fact, this is regarded a reliable source of mortality data when deaths are certified by a medical practitioner, with reported causes of death conforming to the uniform coding of the International Classification of Diseases (ICD) (Parkin, 2006a). Despite about 42% global vital registration coverage as at 1990, the current coverage in Africa has been reported to be incomplete and implausibly low (Parkin, 2001).

Cancer contributes hugely to the public health burden in Africa. Yet, due to data gaps, the exact burden is still far from known. With continued urbanization,

population growth and increasing life expectancies in Africa, the burden of cancer is still expected to increase. The response from the government of many African nations still remains a huge concern. There is need for urgent re-prioritization of health programmes in Africa towards improving research and training, screening, diagnosis and treatment, cancer registration and data handling, and the overall management of cancer in the region.

4.4 CHRONIC RESPIRATORY DISEASES

4.4.1 Chronic Obstructive Pulmonary Disease (COPD)

Emanating evidences from the literature search suggest there may be on-going efforts to estimate the prevalence of COPD in Africa (and or sub-Saharan Africa) by other researchers, among which the BOLD initiative is particularly a leading research group (Burney, 2011). This study, however, to my best knowledge, provides the first systematic continent-wide estimates of COPD prevalence in Africa. The results show an internal consistency and homogeneity among spirometry-based data set, which was further supported by a significant association between patient's age and COPD prevalence in the spirometry-based data set, as observed across many studies (Chan et al., 2012, Mufunda et al., 2006a, Silva-Matos and Beran, 2012a, Lopez Varela et al., 2010). Moreover, the analysis points out statistically significant differences between spirometry and non-spirometry data.

One major population based COPD survey conducted in Africa was the 2006 BOLD study, which was actually conducted across 12 sites globally. The study reported a global COPD prevalence of 10.1% (male 11.8%; female 8.5%) using GOLD criteria (Buist et al., 2007). The study did not quote overall estimates for Africa, as South Africa the only study site in Africa. However, among men and women aged ≥40 years in South Africa, the study reported a COPD prevalence of 22.2% and 16.7%, respectively (Buist et al., 2007). This estimate seems high and it is very unlikely to be representative of the rest of the African population.

In other studies conducted among community-based population samples, a spirometric prevalence of 13.6% was estimated in Malawi in 2001 and 9.2% in Algeria in 2009 (Fullerton et al., 2011, Khelafi et al., 2011). Other studies conducted in Africa were mainly non-spirometric with relatively low prevalence rates reported, asides from studies in occupational settings which had higher prevalence rates, possibly due to repeated exposure to risk factors in these settings. For example, Nigeria recorded a prevalence of 5.6% and 1.7% in 2009 and 1999 respectively, and South Africa recorded a prevalence of 2.6% in 2004 (Desalu, 2011, Ehrlich et al.,

2004, Khelafi et al., 2011). These studies, albeit, are the major population-based studies on COPD conducted in Africa, with none of these reporting a systematic continent-wide COPD prevalence estimate.

In the current study, the reported mean and median prevalence rates from all study populations were higher for the spirometric studies compared to non-spirometric (other) studies (**Table 3.31**), which thus supports previous reports on the under-estimation of COPD from non-spirometric studies (Buist et al., 2007). Although, the gender based differences for both spirometric and non-spirometric studies were not statistically significant, spirometry studies recorded higher COPD prevalence rates (mean and median) among men, which has been observed across many population based surveys (Buist et al., 2007).

Meanwhile, from the 2010 Institute for Health Metrics and Evaluation (IHME) global burden of disease estimates, chronic respiratory diseases overall burden have been decreasing globally, responsible for about 4.7% of global disability adjusted life years (DALYs) in 2010 (Murray et al., 2012). Their analysis further revealed the DALYs and deaths for COPD decreased between 1990 and 2010 by 2.0% and 6.4% respectively (DALYs decreased from 78.3 to 76.7 million, and deaths from 3.1 to 2.9 million) (Lozano et al., 2012, Murray et al., 2012). These are global estimates which are based on complex modelling, and that these may not necessarily reflect the COPD prevalence in many parts of Africa for several reasons, including (but not limited to) contextual, socio-economic, demographic and ethnic differences across many regions of the world. Moreover, concerns have been raised about the choice of data and modelling methods used in the GBD 2010, estimates should therefore be treated with caution until they are individually confirmed (Fan and Lam, 2012, Whiteford et al., 2013). In sub-Saharan Africa however, IHME estimated that DALYs from COPD increased from 4.8 million in 1990 to 5.7 million in 2010 (18.8% increase), while deaths decreased by 1% from 70 thousand to 69.3 thousand over the same period, respectively (Murray et al., 2012, Lozano et al., 2012).

COPD and smoking

Across retained studies, four studies reported COPD risks among current smokers (Buist et al., 2007, Desalu, 2011, Musafiri et al., 2011b, Ayo-Yusuf et al., 2008). Based on these studies, it was observed that the prevalence of smoking was high in some study populations, and with odds of having COPD among current smokers estimated at 6.37 (Nigeria), 3.22 (Rwanda), and 1.15 and 2.84 (South Africa) (Buist et al., 2007, Desalu, 2011, Musafiri et al., 2011b, Ayo-Yusuf et al., 2008) (**Table 4.5**). Conclusions drawn from this must be interpreted with caution, as this study is not a comprehensive review of smoking prevalence in Africa, moreover, there were only four studies reporting COPD risks among current smokers (Buist et al., 2007, Desalu, 2011, Musafiri et al., 2011b, Ayo-Yusuf et al., 2008).

Table 4.5. Prevalence of COPD in terms of smoking from selected studies

Author	***Study setting***	***Sample size***	***COPD prevalence (%)***	***Current smokers (%)***	***Odds ratio of COPD among current smokers (95% CI)***
Ayo-Yusuf et al. (33)	Mixed	4464	3.2	7.3	2.84 (1.60, 5.04)†
Buist, A.S. et al. (23)	Mixed	847	23.8	30.0*	1.15 (1.00, 1.32)**
Desalu OO (24)	Rural	391	5.6	2.6	6.37 (2.12, 19.4)
Ehrlich, R.I. et al. (26)	Mixed	13468	2.6	21.7	-
Gathuru, I.M. et al. (28)	Urban	270	9.5	10.8	-
Musafiri, S. et al. (30)	Mixed	1824	4.5	16.7	3.22 (1.53, 4.31)

*†odds ratio in women, *20 pack years, **10 pack years*

However, some authors have warned that Africa is on the verge of a smoking epidemic due to a rapidly spreading tobacco market in the region, and this could be contributing to the rising burden of COPD in the continent (Jagoe et al., 2002). For example, in 1995, Jha and colleagues reported an increasing prevalence of smoking in Africa with an overall prevalence estimated at 18% (Jha et al., 2002). Between 1996 and 2005, a systematic review of studies conducted among persons aged 15 years or more, across 14 countries in sub-Saharan Africa (SSA), reported smoking prevalence ranging from 6% to 24%, with the prevalence significantly higher among young smokers (aged 18-25 years) (Townsend et al., 2006). In 2006, a demographic health survey, which was also conducted across 14 countries in SSA, further supported this increasing smoking prevalence in Africa, with reported smoking prevalence ranging from 8% to 27% (Pampel, 2008). Moreover, some other research findings have shown that COPD prevalence in many parts of the world increases along with the increasing number of cigarette packs per year, with findings in some African population groups suggesting these populations could be more prone to the health risks from tobacco smoke than people living in other parts of the world (van Gemert et al., 2011, Buist et al., 2007, Chatila et al., 2004).

Study limitations

This study aimed to provide an evidence-based and data-driven prevalence estimate of COPD in Africa, however, the current low research output and the major gaps in data availability from many countries have greatly limited the analysis. It is therefore understandable there could be uncertainties surrounding the estimates of the prevalence of COPD, such as variations in population structures, diagnoses, sampling methods, and effects of other health determinants (beyond the age of patients).

First, the number of retained studies was very low. Only 8 African countries were represented, and over 50% of data-points originated from South Africa and Nigeria. The results may therefore tend to reflect more the COPD burden in these two countries. In addition, given that these two are relatively wealthy countries in African terms, this may limit their generalizability to other African countries. Second, the overall sample size (at 24,747) was relatively small, with a mean and median sample

size per study of 1,767 and 416, respectively. Indeed, I cannot say with all certainty how closely representative these estimates were of the larger African population. Third, there were significant variations in diagnostic criteria and survey methodologies across studies. Although, most retained studies were population-based cross-sectional studies, however, due to the very limited population-based evidence in Africa, and due to the published reports that occupational COPD contributes significantly to the global burden of COPD (Boschetto et al., 2006), studies conducted in occupational settings were also retained. Inclusion of these occupational studies may potentially the analysis, as this is strictly within a population where subjects have been exposed over time to COPD risks. Additionally, there were only 13 studies retained in total, with only 5 based on spirometry. Due to these few studies retained and significant heterogeneity between studies, no pooled prevalence rate was estimated (COPD cases were mainly based on median and inter-quartile range from the studies). This therefore limited the overall analysis of the study, thus making interpretations very difficult. Finally, data on age- and sex-specific prevalence, including corresponding data on urban-rural settings were not always provided across all studies, despite these data being of vital importance to perform further comparisons and reach conclusions about the prevalence of COPD in specific age groups or settings.

Public health response to COPD in Africa

The relative neglect by the governments of many African nations has posed a major obstacle to the fight against the growing burden of COPD in Africa (van Gemert et al., 2011). COPD is thought to be a rather complex disease, usually self-inflicted, irreversible, and difficult to treat (Barnes, 2007, Bousquet et al., 2010), thus, many African governments have not set up awareness campaigns and preventive programmes that can help address the disease (Chan-Yeung et al., 2004).

The challenges arising from unchecked urbanization in many African countries, with no policies and or legislation to protect citizens from adverse effects, such as increase tobacco sales and use, and air pollution from industrial effluents, smoke and smog, have also contributed to the growing burden of COPD (van Gemert et al.,

2011). For example, a study showed that less than 10% of the population in developing countries, especially in Africa, is fully protected by any form of tobacco-demand reduction measures (Barnes, 2007). As noted above, instituting effective tobacco control measures is even more difficult because tobacco companies, which sometimes may be important drivers of some African economies, are using several tactics to resist regulation against its products (Otañez et al., 2009). In the global market, these companies stress the importance of tobacco to the economy of the countries that grow it, fund political parties, lobby and influence policies on tobacco products, prevent anti-smoking adverts and campaigns, and buy off researchers and experts to create controversies on established facts on smoking (Otañez et al., 2009, Saloojee and Dagli, 2000).

Research findings have further shown that the risk of developing COPD from exposure to biomass fuels is comparable to the risk from tobacco smoking (Ait-Khaled et al., 2001, Kiraz et al., 2003). This is particularly significant in Africa, as about 90% of rural dwellers still rely on unprocessed biomass fuel for domestic cooking and heating, a situation that has been made worse due to inadequate health awareness and intervention programmes reaching these settings (Desalu et al., 2010). In fact, emerging evidence now suggest that due to erratic power supply and high costs of cooking gas in many African nations, the use of charcoal and firewood is gradually increasing among many urban dwellers, as this is now considered a cheap alternative for domestic cooking (Musafiri et al., 2011a).

On the interventions for COPD in LMIC, research evidences suggest that an improved biomass stove and cooking environment remain the most cost-effective intervention for reducing the prevalence COPD in sub-Saharan Africa (van Gemert et al., 2011). There are established reports that health sector reform programmes targeted at COPD and other chronic diseases in many African countries have not been very effective (Abdool-Gaffar et al., 2011, Aisanov et al., 2012). The Global Alliance against chronic Respiratory Diseases (GARD), an initiative of the WHO, recommends that a framework for chronic respiratory diseases surveillance should involve monitoring the exposures, outcomes and health system capacity response,

and technically supporting appropriate interventions as the need may be required (Bousquet et al., 2010). However, according to WHO African Regional Office, GARD functions in Africa, but insufficient government support at many country levels often leads to non-implementation of programmes (WHO Regional Office for Africa, 2006, van Gemert et al., 2011). In addition, while appreciable health reforms and intervention programmes have been conducted in some parts of Africa, adherence to these programmes at a community and individual level is low (Musafiri et al., 2011a). For example, biomass stove intervention programmes in some areas have not been effective; reports show there are a wide range of national, regional, community and individual reasons why people may not adhere to the intervention programmes (Stanciole et al., 2012). This further underscores the importance of understanding cultural backgrounds and social systems in an African setting towards improving acceptability of many interventions (Musafiri et al., 2011a, Stanciole et al., 2012).

The delayed health care seeking behaviour in many African populations has also affected the management of COPD (van Gemert et al., 2011). For example, in a study of 298 patients attending respiratory clinics in rural South Africa, the observed median total delay to health facility was about 10 weeks, despite many being at severe stages of disease (Pronyk et al., 2001). This has been linked to high cost of health care, illiteracy and inherent cultural beliefs, with all these resulting in increased patronage of traditional (herbal) healers (Chan-Yeung et al., 2004). Patients often present back at health centres with complications from improper management given by the traditional healers (Ait-Khaled et al., 2001). In health service delivery, studies have reported that many health workers are ill-equipped in diagnosing COPD, making the under-diagnosis of COPD a problem confronting many African nations (Martins et al., 2009). Moreover, it is believed that the under-recognition of COPD in African countries may be because patients present late and, even after presentation to health services, diagnoses are typically delayed until the disease is relatively advanced (Martins et al., 2009, Menezes et al., 2004). Research findings have shown that lack of (use of) spirometers poses a very important practical challenge in rural settings with the main reasons being due to unavailability,

improper usage, and low awareness of their importance (Mehrotra et al., 2009). The unavailability and unaffordability of drugs have also affected health service delivery (van Gemert et al., 2011). Many countries provide free tuberculosis and HIV treatments, while essential drugs for COPD and other CRDs, such as inhaled beclomethasone, are either unavailable or unaffordable (Ait-Khaled et al., 2007a). This unavailability of drugs may reflect lack of funds but may also be partly due to available limited funds being used inappropriately for expensive drugs that have no proven value in the management of COPD (van Gemert et al., 2011). The relatively low income status in Africa is also contributory to the overall burden of COPD in Africa, especially at the family and individual levels. According to clinicians, poor living conditions, such as overcrowded homes, poor domestic cooking environment, and poorly ventilated houses, may worsen COPD; and due to the low income status, patients may still lack the financial resources to seek proper treatment (Poyser et al., 2002). Personal healthcare expenses in Africa are mostly out-of-pocket; there are no standard health insurance schemes as found in high-income settings (Stanciole et al., 2012).

The low level of published research on COPD and other CRDs has posed a major challenge to policymakers and many stakeholders (de-Graft Aikins et al., 2010b), as there are not yet enough evidence-based findings that can contribute to informed policy making to tackle this disease burden (Mehrotra et al., 2009). The limited amount of published research in Africa may be partly due to challenges in conducting studies that would fully adhere to internationally agreed case definitions (Martins et al., 2009). For example, many studies now use post-bronchodilatory spirometry as a gold standard (Buist et al., 2007); whereas others state that using post-brochodilator estimates may result in a 5-50% reduction in prevalence compared to pre-bronchodilator values (Lopez Varela et al., 2010). It has been suggested that the low research output reflects the poor recent availability of research funding for COPD by funding agencies, which in turn reflects their lack of priority given to COPD (Mehrotra et al., 2009, Abdool-Gaffar et al., 2011). The research priorities of many African governments still focus on communicable diseases, notably HIV/AIDS, tuberculosis and malaria (de-Graft Aikins et al., 2010a). In

addition, the influence of the tobacco industry, which financially supports many governments in Africa, may also have negatively affected research output in the field (van Gemert et al., 2011, Sitas et al., 2004, Adejuwon, 2009).

With the few published studies only available from some countries in Africa, the problems of data availability on COPD still persists. However, it is evident from the few studies that the burden of COPD in Africa is significant. With continued urbanization, rapid ageing and lack of corresponding measures to check the effects on the population, the burden of COPD will continue to grow and it is set to become one of the major public health problems in Africa.

There is need for more research on COPD prevalence, incidence, sequelae and mortality, along with well-designed trials, to identify how to effectively reduce risks from exposure to biomass fuels and tobacco smoking. With improved awareness of this problem, policy makers and governments of many African nations should give more attention to NCDs such as COPD, fund relevant research to improve evidence for decision making, and thus make informed decisions on preventive and treatment strategy options, and so help counter the rising disease burden over the next decade.

4.4.2 Asthma

This study, to the best of my knowledge, provides the first systematic, data-derived and continent-wide estimates of asthma prevalence in Africa. The modelling was based on published epidemiological data on "current wheeze" prevalence, which has relatively higher sensitivity and specificity (Burney et al., 1989, IUATLD, 2011), and also shows a significant association between age and asthma prevalence (Murray et al., 2012).

As noted earlier, based on the 2010 IHME GBD estimates, the overall burden of chronic respiratory diseases have been decreasing globally, responsible for about 4.7% of global disability adjusted life years (DALYs) in 2010, with asthma accounting for about one-fifth of this (Murray et al., 2012). However, the IHME reported that DALYs from asthma increased by 4.6% (from 21.5 to 22.5 million) between 1990 and 2010, while deaths decreased by 9.1% (from 0.38 to 0.34 million) over the same period globally (Lozano et al., 2012, Murray et al., 2012). It may be inappropriate to compare these estimates with the current estimates, as these are global estimates and have very different contexts from Africa. Concerns have been raised about the application of non-user friendly analytical methods, heavy statistical modelling, and difficulties in assessing the design methodologies and metrics used (Fan and Lam, 2012, Whiteford et al., 2013). In sub-Saharan Africa however, IHME estimated that DALYs from asthma increased from 3.2 million in 1990 to 4.0 million in 2010 (25% increase), while deaths decreased by 1.8% from 39.8 thousand to 39.1 thousand over the same period, respectively (Murray et al., 2012, Lozano et al., 2012).

In Africa however, the ISAAC study group, which mainly conducted epidemiological studies on asthma, reported increasing prevalence rates of asthma across many study settings in Africa (Ait-Khaled et al., 2007b). For example, the prevalence of "current wheeze" (wheeze at rest-12 month) among children aged 13-14 years old in South Africa increased from 16.1% to 20.3% between 1995 and 2002 respectively; Nigeria (West Africa) recorded an increase from 10.9% to 13.0%, Ethiopia (Horn of Africa) reported an increase from 6.2% to 9.1%, and Kenya (East

Africa) increased from 13.9% to 18.0% (Ait-Khaled et al., 2007b, Zar et al., 2007). The current pooled crude prevalence rates also reflect this, with a prevalence of current wheeze (wheeze at rest- 12 month) at 13.5% and cumulative prevalence of asthma at 9.5% (**Table 3.40)**. Furthermore, in keeping with findings from many studies, the pooled crude prevalence rates were consistently higher in urban than rural settings (**Table 3.39**), suggesting the effects of increasing urbanization on asthma prevalence in Africa (Odhiambo et al., 1998).

From the modelling, a prevalence of 7.0% was estimated for asthma in Africa in 2010 among people under the age of 45 years, equivalent to about 30 million people, with children <15 years accounting for 51% of those affected. However, in the modelling, the R^2 was just about 2%. This is very low, and may reflect the challenges with the conduct of asthma research in an African population. First, the model was based on the symptom '*wheeze at rest*'. Even with this symptomatic definition, authors still complained it was difficult to distinctly classify people as having asthma. In addition, the symptoms of asthma has been said to overlap with COPD and respiratory allergies. However, as noted in preceding sections, a low R^2 may not mean the model is not well-fitted (Oles et al., 2012). The argument is that R^2 may not indicate whether a model is adequate, and in such instances a good model may present with a low R^2 and a poor model may have a high R^2 (Higgins et al., 2009). Many have also reported that R^2 is more appropriate for linear regression (Oles et al., 2012, Higgins et al., 2009). A detailed discussion on R^2 has been included earlier under *hypertension discussion*. Meanwhile, the model showed an increasing asthma prevalence from early childhood (3.2%) up till age 15 years (9.6%), where a gradual decrease in prevalence declining to 1% at 45 years. This model shows a prevalence trend that has been reported in some studies, as early childhood has been reported as a stage when asthma is most prevalent in many settings (Zar et al., 2007). However, the inability of the model to appropriately account for urbanization, atopic sensitizations, pollution, second hand smoke in children, among other determinants of asthma, are important factors for consideration. As noted, it is important not only to look at the R^2 and how well the model fits the data, but also to closely if this is a reasonable prediction in a scientific context (Cameron and Windmeijer, 1995).

To the best of my knowledge, there are no direct comparable estimates of the prevalence of asthma in Africa; however, public health experts have reported that increasing tobacco smoking without appropriate legislation and implementation of relevant health promotional measures in Africa may be responsible for the increase in asthma and other chronic respiratory diseases' burden in the region (Odhiambo et al., 1998). Passive smoking among children is a confirmed risk for asthma in this age group (Odhiambo et al., 1998), and could possibly account for the higher cases of asthma among children <15 years reported in the current study. In addition, the Global Burden of Asthma Report (GBAR) reported an increasing trend of asthma globally (Braman, 2006). GBAR estimated over 235 million asthma cases worldwide, and about 50 million people living with asthma in Africa in 2004, with the highest prevalence (8.1%) recorded in South Africa (Braman, 2006). The authors argue that this increasing trend is expected due to rise in atopic sensitizations, allergic conditions, and changing patterns of environmental triggers (associated with environmental smoking exposure in children, population growth and urbanization) in Africa over the last two decades (Braman, 2006). These factors may therefore be indicative of the current reported high estimates in Africa.

Study limitations

While the aim of this study was to provide an improved prevalence estimate of asthma in Africa by carefully selecting high quality studies and applying simple analytical tools, there are however factors that could have affected the analysis. Variations in population settings, diagnostic criteria, sampling strategies, and effects of other health determinants (beyond age of patients) are factors that need be considered. First, as noted in the methods single age (usually mean age) was mostly employed in the modelling. None of the selected studies reported age specific estimates, as the studies were mainly in the children and adolescents. In fact, working on a data with 5-year age specific estimates in children would have made the modelling more representative of all included study populations. This could have therefore been a limitation in this study.

For the pooled asthma prevalence, I^2 was 99.2%. This implies that there is very high heterogeneity across selected studies; and at $p<0.0001$, this is statistically significant. There is therefore strong evidence against the null hypothesis that studies are evaluating the same effect. For a combination of studies with such high heterogeneity, it may also not be appropriate to pool a summary effect. However, as reported earlier, there is very low research output in Africa, and the few studies have not been conducted under strict international guidelines, so heterogeneities can be expected. In addition, restricting my analysis to studies that have the same study design, same sampling frame and same case definition is almost impossible.

The variation in diagnostic criteria was observed across many study settings, with criteria based on asthma symptoms and ISAAC scores frequently used. This could have reflected in the reported high estimates of asthma in Africa, as there are evidences suggesting the ISAAC studies could have over-estimated the prevalence of asthma in Africa, as most study centres were mainly urban; and with ISAAC studies conducted mainly in the age range 13-14 years, it may still not be representative of all age-groups and the overall population (IUATLD, 2011, Patel et al., 2008). Still on the ISAAC studies, two ISAAC studies (ISAAC I and III) (Ait-Khaled et al., 2007b, Zar et al., 2007), included in the analysis were conducted across many countries in

Africa and provided about 50% of the total 64 data points in this study. Second, while many studies were cross-sectional population-based, studies conducted in occupational settings were also included, as contained in the quality criteria and grading. This is in view of reports revealing that occupational asthma contribute significantly to the global burden of chronic respiratory diseases (Mengesha and Bekele, 1998, Hnizdo et al., 2001). As these studies reported high prevalence rates, I understand these could have increased the current estimates, too. Third, despite included studies spreading across most parts of Africa (24 countries in total), there are still many countries in Africa that are not included in the review. This reflects data gaps in the continent, and thus the generalizability of these estimates for Africa may need to be cautiously interpreted. In addition, the total sample size of 187904 (from all studies) may not be a representative sample of the general African population as there were younger age groups. Indeed, I cannot say with all certainty how closely representative these estimates were of the larger African population. Finally, data on age- and sex-specific prevalence, including corresponding data on urban-rural settings, which are vital comparative indices in any study, were not always provided across many studies.

Public health response to asthma in Africa

It is important to note that chronic respiratory disease burden, including asthma have continued to increase in Africa due to lack of appropriate response from the governments of many African countries (Ait-Khaled et al., 2001). The national emphasis on asthma and relevant health messages have been sub-optimal, leading, in sequence, to poor awareness of the burden, low prioritization, inadequate staffing and resources, and very low budget allocation. In fact, budget allocation in many African countries mainly targets infectious diseases; funds have been greatly biased towards HIV/AIDS, malaria and tuberculosis, as these are the main government priorities (Bahadori et al., 2010, Beaglehole, 2011). The GBAR authors reported that poor government allocation of funds for asthma remain an important factor responsible for limited access to asthma medications, emergency health care and other related health services in Africa (Braman, 2006). In addition, with tobacco

companies still supporting many African governments, tobacco products' sales have increased, and government funds have remained unavailable for research on asthma, as researches aimed at improving management of asthma may be against tobacco sales and consumption (Musafiri et al., 2011a). This has greatly resulted in increased smoking (without a counter legislation) and a growing burden of asthma, especially among children in Africa over the last two decades (van Gemert et al., 2011). For example, Mackay et al. reported that a comprehensive smoke free-legislation was important to achieving reduction in the incidence of asthma among people without occupational exposure to environmental tobacco smoke. Following the implementation of this legislation in Scotland, a reduction of 18.2% per year was observed in asthma hospital admissions in Scotland among children <15 years in 2009 compared to a mean increase of admission of 5.2% per year before implementation of the legislation in 2006 (Mackay et al., 2010)

The diagnosis and treatment of asthma still remains a major challenge in Africa (Martins et al., 2009). Distinguishing asthma from other obstructive airway diseases has posed a clinical challenge to clinicians (Bousquet et al., 2010). Epidemiological data have shown that while asthma presents in episodes, usually among non-smokers and onset before 40 years, chronic obstructive pulmonary disease (COPD) is associated with smokers, people aged 40 years and above, with symptoms being persistent and progressive (Bousquet et al., 2010, IUATLD, 2011). In practice, asthmatics who smoke may have non-reversible airflow limitation, and some COPD patients may be non-smokers having reversible airflow limitation (Jindal et al., 2006). In addition, many African countries have no standard protocols for the diagnosis and management of asthma (Musafiri et al., 2011a); where these are available, guidelines are rarely implemented, and for the few implemented guidelines, treatment often do not reach the rural population that are mostly affected (Ait-Khaled et al., 2007a). In fact, inaccessibility to healthcare services in many rural and resource-poor African settings often gives traditional healers undue significance in the management of many chronic diseases (Musafiri et al., 2011a). The non-availability and unaffordability of inhaled steroids, and the relative non-adherence to these medications (when available) have also had large negative impact on the

success of the response to asthma in Africa. Studies have shown that about 50% of people adhere to prescribed medications (Ait-Khaled et al., 2007a, Salama et al., 2010). Reasons for non-adherence include side-effects, dosing frequencies, and lack of patient education on their illness, need for treatment and how to take medications (World Health Organization, 2012). There are also inherent socio-cultural misconceptions and individual values that need to be understood and addressed toward improving the acceptance and use of asthma medications (Zaraket et al., 2011), with continual public awareness and education being advocated, especially among parents of children with asthma (Zaraket et al., 2011, van Gemert et al., 2011).

Asthma is an important and increasing public health problem in Africa which receives inadequate priority and attention. With increasing urbanization, population ageing and adoption of western lifestyles in many African settings, these trends are set to continue in the near future. There is need to identify and prioritize feasible strategies that can be adopted to promote the implementation of effective interventions that will address this increasing burden in Africa. There is a need for African national governments to also consider effects of associated risk factors in public health policy planning on this topic with a focus on reducing environmental triggers, placing restrictions on tobacco adverts, and appropriately educating healthcare personnel and the public on the management of the disease and the preventive measures.

One vital point from the findings and discussions is the growing burden of NCDs in Africa, yet, I still cannot say with all certainty how representative my estimates are of the African population. A poor response from the government of many African nations has also not helped in addressing this burden. Other challenges include (but not limited to) those associated with diagnosis of these diseases, inadequate health workforce, poor funding of the health system, and low socio-economic status. On the conduct of this research, the lack of data on many NCDs was a major limitation. And in cases where data exist, they are often incomplete and unreliable, making the estimation of the disease burden almost impossible.

5 CONCLUSION

In this thesis, I attempted to review available evidence on four major NCDs in Africa towards providing close population representative continent-wide estimate of the prevalence and/or incidence of these diseases in Africa. Let me point out here that I still cannot say with all certainty how representative these estimates are of the African population. In this concluding chapter, I will summarise my overall observations and discuss recommendations based on my findings.

5.1 Summary of Observations

The prevalence and/or incidence of some NCDs reported in this thesis were comparable with some of the WHO estimates on NCDs for Africa (**Table 5.1)**. There were however some few differences, which a number of factors could have accounted for. As noted in the introduction, top among these is the fact that some of the WHO GBD estimates on Africa have been based on an extrapolation and over-modelling of the very limited data on NCDs in Africa (King and Bertino, 2008). Additionally, some authors have possibly derived their estimates by modelling from other non-African countries and imputing these into a template for African countries (Fan and Lam, 2012). This was also reported by the former Health Metrics Network, which stated that many of the global and regional estimates of disease burden were based on advanced statistical modelling rather than through a detailed analysis of empirical data (World Health Organization, 2014a). In addition, most of these estimates were driven by the needs of the donors rather than that of the population the research was primarily conducted (World Health Organization, 2014a). For effective policy response, these estimates may need to be carefully interpreted, especially with regards to population representativeness.

Meanwhile, some estimates in this thesis were relatively higher than some of those reported in other world regions. For example, in comparison to other regions of the WHO, the incidence of cervical cancer in Africa reported in this thesis was the highest, and the prevalence of hypertension was the second highest (**Table 5.1**). This observation may be vital to the high burden of NCDs in Africa noted by previous reports, and may thus point to the need for African nations to address NCDs more keenly.

Table 5.1. Summary of prevalence/incidence rates for some NCDs in WHO regions

NCD	*Current study (95% CI)*	*Africa∞*	*The Americas∞*	*Eastern Mediterranean∞*	*Europe∞*	*South East Asia∞*	*Western Pacific∞*
Hypertension†	25.9 (23.5, 34.0)	27.0	21.0	23.0	36.0	19.0	19.0
Diabetes†	4.0 (2.7, 6.4)	4.0	10.0	17.0	12.0	17.0	7.0
Cervix*	28.2 (22.1, 34.4)	30.7	15.3	9.0	10.1	24.4	-
Breast*	17.7 (13.0, 22.4)	26.5	57.2	29.3	62.8	26.1	26.3
Prostate*	14.5 (10.9, 18.0)	20.4	66.7	12.0	55.3	-	-
Kaposi*	14.3 (11.9, 16.7)	7.6	-	-	-	-	-

*†prevalence in percentage, *incidence per 100,000 person years*
∞ published age-standardized estimates for 2008
Source: WHO Global Burden of Disease 2008 and GLOBOCAN 2008

One major observation is the dearth of data on NCDs across Africa. According to the UN, there are 54 fully recognized sovereign states (countries) in Africa (United Nations, 2014). Excluding the searches on hypertension and diabetes, which relatively had higher number of studies, most data from other NCDs reviewed came from less than 50% of all African countries. For example, studies on stroke were conducted in 10 African countries, cancer in 20 countries, COPD in 8 countries, and asthma in 24 countries (**Table 5.2**). This dearth in data has been noted generally among public health experts (Alwan et al., 2010). As discussed earlier, Holmes and colleagues reported that up till 2009, there were 14 publications on stroke in Africa, accounting 0.06 publications per million people with stroke in Africa, and this only

representing 0.6% of the total publications on stroke in the United States (Holmes et al., 2010). Publications on diabetes in Africa were 84 for the same period, accounting for 7 publications per million people with diabetes in Africa, and this represents 8% of the total publications on diabetes in the United States (Holmes et al., 2010).

Table 5.2. Number of studies retained and African countries involved

NCD	***Studies retained***	***Countries of selection***
Hypertension	92	31
Stroke	19	10
Diabetes	48	28
Cancer	39	20
COPD	13	8
Asthma	45	24

An analysis of retained studies according to their respective study periods revealed that most studies were conducted between 2000 and 2013. The main exceptions were observed in the stroke and cancer reviews, where most retained studies involved collation and analysis of data from stroke and cancer registries over longer study periods (**Table 5.3)**. Nonetheless, this observation generally shows a gradual increase in NCD research in Africa. It could also show that the relative poor public health response to these diseases in the continent may be due to the observed low level of research in the preceding years.

Table 5.3. Number of retained studies by study period

NCD	***1980-89***	***1990-99***	***2000-13***
Hypertension	5	13	74
Stroke	7	3	9
Diabetes	4	13	31
Cancer	7	17	15
COPD	0	4	9
Asthma	1	20	24

A major observation on the lack of data was revealed from the review on COPD. Following the literature search, there were only 5 spirometry-based studies on COPD retained. It is appalling that despite previous studies reporting that COPD is among the leading causes of deaths globally and the burden in many African countries is rising (Buist et al., 2007, Musafiri et al., 2011a, Mehrotra et al., 2009), it has yet to generate interest among African researchers. In fact, the policy response to COPD in many African countries has been affected by this gap.

Another factor that could have affected the research output in Africa could be challenges associated with case ascertainment, disease measurement and study designs. For all the NCDs reviewed, excluding hypertension, this was a major limitation. Epidemiologists, clinicians and health workers find it difficult to diagnose some medical conditions. International diagnostic guidelines, which can be of assistance, are hardly adhered to, especially due to lack of proper training and medical equipment (Martins et al., 2009). The relatively high number of studies on hypertension may be due to the ease of conducting basic blood pressure measurement, as reports show that this is among the simplest medical investigation carried out by an average health worker in many African settings (Addo et al., 2007).

The role of international advocacy on certain NCDs, the global recognition NCDs attract, and interests from potential funding organizations may have also resulted in the dearth of data on NCDs in Africa. Prior to the UN 2011 high level meeting on NCDs, researchers have mainly focussed on infectious diseases. The reason obviously due to the better recognition infectious diseases receives globally and the funding it attracts. As noted in the introduction, a review of World Health Assembly (WHA) resolution from 1948 to 2013 revealed that of the total 484 resolutions made by WHA, 368 (76.0%) were on infectious diseases, 99 (20.5%) on NCDs and 17 (3.5%) on both (World Health Organization, 2014e, World Health Organization, 2014d). However, this trend is gradually changing, as experts believe the awareness on NCDs has improved, and about 50% projected increase in NCDs research may be expected from 2015 to 2025, as compared to what was observed before 2010 (Horton, 2013).

Meanwhile, the distribution by African sub-regions across retained studies suggests the level of NCD research in western Africa is more than in other parts of Africa (**Table 5.4**). This is particularly important with regards to the estimate provided in this study. The estimates may reflect more the burden of NCDs in this African region, and its generalizability to other parts of the African continent may need to be carefully interpreted.

Table 5.4. Number of retained studies by African sub-regions

NCD	***Central***	***East***	***North***	***South***	***West***	***Horn of Africa (excluding Ethiopia)***
Hypertension	7	21	12	15	43	1
Stroke	0	3	7	4	5	0
Diabetes	4	9	7	12	6	0
Cancer	3	5	11	11	9	0
COPD	1	1	3	5	3	0
Asthma	2	8	5	12	18	0

The relative lack of studies from the Central African region and the horn of Africa (excluding Ethiopia) was another observation. This obviously reflects very low level of research in this region, particularly in the Central African Republic, Equatorial Guinea, and Sao Tome and Principe in central Africa; and Djibouti, Somali and Eritrea in the horn of Africa (**Tables 5.4** and **5.5**). One factor that could be affecting the conduct of research in these regions may be due to political instability in some of these countries (Dalal et al., 2011). For example, Central African Republic, Somali and Eritrea have all witnessed major civil unrests in the last 10-20 years. This may not be applicable to countries like Niger, Sao Tome and Principe, Botswana and Lesotho, which have experienced relatively smooth political transition in the last 10 years. No doubt, these countries might be having some other issues, including, but not limited to poor socioeconomic status, educational system, and health system, respectively. This observation may therefore point to understanding and addressing

the mechanisms needed to strengthen research capacities more keenly in countries generally undergoing some difficult circumstances.

Table 5.5. Distribution of countries without studies

African region	***Countries without studies***
Central	Central African Republic, Equatorial Guinea, Sao Tome and Principe, Burundi*, Chad†, Gabon†
East	Comoros, Djibouti, Somali, Eritrea*, Seychelles†
North	Libya†
South	Lesotho, Botswana, Swaziland*
West	Niger, Mauritania, Cape Verde*, Mali†

*†one study, *two studies*

Inequity in the conduct of research and availability of data on NCDs was another major point observed. While most studies were conducted in urban big cities, or generally in a mixed population settings, the coverage of rural populations was remarkably low. Hypertension studies had a fair coverage among rural dwellers, with 47 rural studies from a total of 92 studies. However, the coverage in other reviews was relatively low. Stroke had 4 rural studies out of 19, diabetes had 18 rural studies out of 48, COPD had 2 rural studies out of 13, and asthma had 3 rural studies out of 45, while cancer had no data from any registry covering mainly rural dwellers (**Table 5.6**).

Table 5.6. Number of retained studies based on study design and settings

NCD	*Total number of studies*	*Number of studies based on original epidemiological surveys*	*Number of studies based on health service records*	*Number of studies conducted in rural settings*
Hypertension	92	92	-	47
Stroke	19	14	5	4
Diabetes	48	48	-	18
Cancer	39	3	36	-
COPD	13	13	-	2
Asthma	45	45	-	3

The distribution of studies appears to reveal a geographical pattern characterized by small clusters of well-researched urban areas surrounded by large under-researched rural areas. While African is experiencing the fastest rate of urbanization worldwide, records show that two-thirds of the African population still reside and work in rural areas (United Nations, 2014). This thus potentially infers that estimates provided by many researchers on the burden of disease in Africa may be mainly representative of the relatively smaller urban areas in the continent, while the rural areas which bear the larger burden of disease may not be well-represented. This equity in research has been noted in a previous study by Rudan and colleagues (Rudan et al., 2005). The WHO believes investing in national health information system with effective data management strengthened from the grassroots may help address this gap (World Health Organization, 2014a).

Across all studies, with the exception of the cancer and stroke review, data originating from health service records were predominantly absent. Data were mainly extracted from original epidemiological surveys of NCDs (**Table 5.6**). In fact, emerging evidence now suggest that some routine health service records may provide better information necessary for the estimation of disease burden than some epidemiological surveys, particularly when there is active registration, monitoring

and evaluation of these records (World Health Organization, 2014b). However, population-based studies have been the hall-mark of many systematic reviews. Estimates are mainly based on deliberate efforts by researchers to ascertain the burden of disease in an area, with very little or no contribution from routine health service records. The implication is that conclusions may be biased, especially when study designs, case definitions and selection criteria do not follow standard protocols. Besides, and just as noted above, their conclusions may be tailored along the interests of the funders of such studies, and may therefore not necessarily provide results that can inform effective public health response. While it is understandable that some national health records and results of some national surveys may actually exist in Africa, the fact that they are not publicly available may still further imply that health management information system are functioning sub-optimally or even non-existent across many African countries.

5.2 Recommendations

Based on my findings in this thesis, I have observed that:

i. the prevalence and/or incidence of the reviewed four major NCDs is relatively high in Africa;

ii. there is low level of research on these NCDs, with research output gradually increasing over the last 10 years;

iii. health service records, which could have been an alternative source of data on NCDs, are virtually non-existent or not publicly available; and

iv. these three above may have contributed to the dearth of data on NCDs at country level, lack of effective policy response to NCDs, and a continued increased in the overall burden of NCDs across Africa.

Hence, what are the feasible options that can effectively address these challenges at various country levels and in the African region at large?

Improvement in country level data through the establishment of a national health management information system may be an important and desirable starting point. However, considering organizational, technical and financial feasibility, this may be difficult to achieve in many African countries. A feasible strategy may be for each African country to adopt a policy that allows the selection of some regional health centres as special health management information centres, with each centre covering a population that is representative of a particular region in the country. Existing structures in these centres may be strengthened, so that data collation, recording, analysis and management may conform to international standards. Health management information specialists may also be assigned to these centres, who can train other health workers on the process of keeping up-to-date health data. Essentially, governments need to create adequate awareness among health workers in these centres and the general public to ensure a smooth conversion. The training of health workers on keeping timely, correct and complete record of health data may further help in sustaining the scheme. Data from these special centres can be

regularly updated and modelled to be reflective of the total country population. Both crude and modelled data can then be incorporated into a national database, and made available to health researchers. There may be need to request technical assistance from the WHO, and also partner with relevant international agencies like the INDEPTH Network, which have been a vital source of comprehensive, longitudinal population data that are generally unavailable in many parts of Africa (Evans and AbouZahr, 2008, Byass et al., 2014). This could further assist in developing this database and ensure better dissemination of data locally and internationally. This may possibly be a long-term solution to the non-availability of data in many African countries.

One other option is a regular conduct of national surveys on NCDs across various country levels in Africa. National surveys on NCDs are currently being carried out in some African countries, but there are concerns on the quality of these surveys and the long periods existing between surveys (Holmes et al., 2010). Essentially, existing national protocols need to be improved, and adhered to international standards, like the WHO STEPwise approach to surveillance (STEPS), which is currently being employed in many countries (Bonita et al., 2013, Hakim et al., 2005). For specific diseases, some surveys already conducted internationally with proven successes that can be adopted by African countries include: the European Community Respiratory Health Survey in Adults (ECRHS) for chronic respiratory diseases, the Burden of Obstructive lung Disease (BOLD) survey for COPD, the International Study of Asthma and Allergies in Childhood (ISAAC) for asthma, the Epidemiological Trial of Hypertension in North Africa (ETHNA) survey for hypertension, and the International Stroke (INTERSTROKE) survey for stroke, among many others. Moreover, under the national survey schemes, periodic calls may be made to health experts within country to conduct original population-based (cohort or cross-sectional) or hospital-based studies on NCDs, across areas where there are limited data on NCDs. Holmes and colleagues already noted that there is need for more longitudinal population-based studies on NCDs in Africa to help in better estimation of disease burden (Holmes et al., 2010). This may also help address inequity in the geographical distribution of research, and all population groups within a country may

be well-represented. Rudan and colleagues noted that special attention must be given to study designs during epidemiological surveys in many under-resourced settings, as this has affected the collation of data on disease incidence (Rudan et al., 2005). Thus, with agreed international standards in design, case definitions, diagnostic criteria and outcome measures, bias and under-reporting may well be avoided.

Another complementary strategy that can improve the response to NCDs in Africa may be for countries to identify existing research centres (or units) focussing specifically on any NCD within the country. Government can then invest in these health centres to improve research outputs and other activities carried out by these research units. Focussed strategies on capacity building within the research units may also be needed, as this can help with improvement in organizational structures, training, performing investigations, and other mechanisms that can promote the conduct of research (Amuyunzu-Nyamongo, 2010).

Within countries, there may be need for a leadership in the health sector devoid of ethnic, religious or political bias. This ensures that the observed gaps and challenges are addressed where and when needed. In addition, a good leadership can help in establishing an effective monitoring, evaluation and surveillance system, where the conduct of research, disease notification, and data collation and registration can be well addressed. This may further help in the sustainability of these strategies.

Population-based interventions targeted at major risk factors of NCDs (tobacco, alcohol, physical inactivity and unhealthy diets) may actually be the needed response in most African countries. However, based on an understanding of the problems highlighted in preceding sections, the needed health information that can inform undertaking these interventions are lacking. However, evidence shows that these interventions may be carried out successfully in a population (Asaria et al., 2007). They are cost-effective, culturally acceptable, and most people including those already suffering from one form of NCD may benefit from it (Asaria et al., 2007). Based on reports, increasing taxes on tobacco and alcohol products are some of the cheapest and most effective interventions for NCDs, and can in fact generate more public funds (Otañez et al., 2009). In many African countries however, achieving this

may be difficult politically due to strong lobbying from companies producing these products, who, in many instances also support the government financially (Alwan et al., 2010). There may be need for strong leadership and high level international partnerships to overcome these difficulties. In addition, experts have advocated for the non-inclusion of industries marketing unhealthy commodities including tobacco, alcohol, and ultra-processed foods, in the formulation of national policy (Boutayeb, 2006, McCarthy et al., 2010).

Largely, all these interventions need adequate funding to be successful on the long term. It has been reported the lack of funds in African countries have affected the sustainability of many interventions for NCDs (Holmes et al., 2010). This is even more marked due to frequent shifts in leadership, political instability and civil unrest (Rudan et al., 2005). As observed in this thesis, a thorough understanding of how to successfully conduct research in difficult circumstances may be needed in most African settings.

In conclusion, I have attempted to give a continent-wide prevalence and/or incidence of major NCDs in Africa. My findings suggest these are relatively high in Africa. However, I still cannot say with all certainty how exact these are in many African countries. There is need for more investment in NCDs research across Africa, especially on mortality, risk factors and other determinants of NCDs in the region. I hope the findings of this thesis will prompt a comprehensive policy response on NCDs across all country level in Africa.

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APPENDICES

APPENDIX 1. Search terms employed on other databases

Appendix 1a. Search terms for studies on hypertension in Africa (EMBASE)

#	***Search terms***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	cardiovascular diseases/ or heart diseases/ or exp hypertension/ or peripheral vascular diseases/
13	Hypertensive heart disease.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
14	12 or 13
15	1 and 11 and 14
16	limit 15 to (humans and yr="1980 -Current")

Appendix 1b. Search terms for studies on hypertension in Africa (Global Health)

#	***Search terms***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp hypertension/ or blood pressure, high/ or high blood pressure/ or hipertensao/ or hypertension arterial/ or exp cardiovascular diseases/ or heart diseases/ or / or peripheral vascular diseases/
13	Hypertensive heart disease.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
14	12 or 13
15	1 and 11 and 14
16	limit 15 to (humans and yr="1980 -Current")

Appendix 1c. Search terms for studies on stroke in Africa (EMBASE)

#	***Search terms***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	stroke/ or brain infarction/ or brain stem infarctions/ or cerebral infarction/ or stroke, lacunar/
13	cerebrovascular accident [Used For] accident, cerebrovascular, acute focal cerebral, vasculopathy, apoplectic stroke, apoplexia, apoplexy, blood flow disturbance, brain, brain accident, brain attack, brain blood flow disturbance, brain insult, brain insultus, brain ischemic attack, brain vascular accident, cerebral apoplexia, cerebral insult, cerebral stroke, cerebral vascular accident, cerebral vascular insufficiency, cerebro vascular accident, cerebrovascular arrest or failure or insufficiency or insult or trauma, cerebrum vascular accident, cryptogenic stroke, CVA, ischaemic seizure, ischemic cerebral attack, ischemic seizure, stroke
14	cerebrovascular disease.mp. (broader terms)
15	CVA.mp.
16	12 or 13 or 14 or 15
17	1 and 11 and 16

Appendix 1d. Search terms for studies on stroke in Africa (Global Health)

#	***Search terms***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	stroke/ or brain infarction/ or brain stem infarctions/ or cerebral infarction/ or stroke, lacunar/ broader terms derrame cerebral
13	cerebrovascular accident/ or intracranial haemorrhage/ or hemorrhagic stroke/ or subarachnoid hemorrhage
14	cerebrovascular disorders [used for] disturbios cerebrovasculares, trastornos cerebrovasculares, broader terms brain diseases
15	CVA.mp.
16	12 or 13 or 14 or 15
17	1 and 11 and 16

Appendix 1e. Search terms for studies on diabetes in Africa (EMBASE)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp diabetes mellitus/ or glucose metabolism disorders/ or disorders of carbohydrate metabolism/ or pancreas islet disease/ or diabetes mellitus, type 1/ or diabetes mellitus, type 2/ or diabetes, gestational/ or diabetic ketoacidosis/ or prediabetic state/ or glycosuria/ or hyperglycemia/ or glucose intolerance/
13	1 and 11 and 12

Appendix 1f. Search terms for studies on diabetes in Africa (Global Health)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp diabetes/ or endocrine diseases/ or glucose metabolism disorders/ or exp diabetes mellitus/ or exp diabetes mellitus, type 1/ or exp diabetes mellitus, type 2/ or exp diabetes, gestational/ or exp diabetic ketoacidosis/ or exp prediabetic state/ or exp glycosuria/ or exp hyperglycemia/ or exp glucose intolerance/
13	1 and 11 and 12

Appendix 1g. Search terms for studies on cancer in Africa (EMBASE)

#	***Searches***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp neoplasms/ or physical disease by etiology and pathogenesis/ or tumour/ exp leukemia/ or exp lymphoma, non-hodgkin/ or exp burkitt lymphoma/ or exp sarcoma/ or exp sarcoma, kaposi/ or exp breast neoplasms/ or exp breast neoplasms, male/ or exp carcinoma, ductal, breast/ or exp "hereditary breast and ovarian cancer syndrome"/ or exp inflammatory breast neoplasms/ or exp gastrointestinal neoplasms/ or exp esophageal neoplasms/ or exp intestinal neoplasms/ or exp colorectal neoplasms/ or exp adenomatous polyposis coli/ or exp colonic neoplasms/ or exp sigmoid neoplasms/ or exp colorectal neoplasms, hereditary nonpolyposis/ or exp rectal neoplasms/ or exp anus neoplasms/ or exp ileal neoplasms/ or exp jejunal neoplasms/ or exp stomach neoplasms/ or exp liver neoplasms/ or exp adenoma, liver cell/ or exp carcinoma, hepatocellular/ or exp lung neoplasms/ or exp bronchial neoplasms/ or exp carcinoma, bronchogenic/ or exp carcinoma, non-small-cell lung/ or exp small cell lung carcinoma/ or exp pleural neoplasms/ or exp pleural effusion, malignant/ or exp solitary fibrous tumor, pleural/ or exp tracheal neoplasms/ or exp uterine neoplasms/ or exp uterine cervical neoplasms/ or exp prostatic neoplasms/ or exp kidney neoplasms/ or exp urinary bladder neoplasms/
13	1 and 11 and 12

Appendix 1h. Search terms for studies on cancer in Africa (Global Health)

#	***Searches***
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp neoplasms/ or cancer (disease)/ or cancers/ or neoplasias/ or neoplasmas/ or tumours/ exp leukemia/ or exp lymphoma, non-hodgkin/ or exp burkitt lymphoma/ or exp sarcoma/ or exp sarcoma, kaposi/ or exp breast neoplasms/ or exp breast neoplasms, male/ or exp carcinoma, ductal, breast/ or exp "hereditary breast and ovarian cancer syndrome"/ or exp inflammatory breast neoplasms/ or exp gastrointestinal neoplasms/ or exp esophageal neoplasms/ or exp intestinal neoplasms/ or exp colorectal neoplasms/ or exp adenomatous polyposis coli/ or exp colonic neoplasms/ or exp sigmoid neoplasms/ or exp colorectal neoplasms, hereditary nonpolyposis/ or exp rectal neoplasms/ or exp anus neoplasms/ or exp ileal neoplasms/ or exp jejunal neoplasms/ or exp stomach neoplasms/ or exp liver neoplasms/ or exp adenoma, liver cell/ or exp carcinoma, hepatocellular/ or exp lung neoplasms/ or exp bronchial neoplasms/ or exp carcinoma, bronchogenic/ or exp carcinoma, non-small-cell lung/ or exp small cell lung carcinoma/ or exp pleural neoplasms/ or exp pleural effusion, malignant/ or exp solitary fibrous tumor, pleural/ or exp tracheal neoplasms/ or exp uterine neoplasms/ or exp uterine cervical neoplasms/ or exp prostatic neoplasms/ or exp kidney neoplasms/ or exp urinary bladder neoplasms/
13	1 and 11 and 12

Appendix 1i. Search terms for studies on COPD in Africa (EMBASE)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	Emphysema or chronic bronchitis.mp
13	copd.mp.
14	chronic obstructive lung disease/ or lung disease/ or obstructive airway disease/ or chronic obstructive lung disorder/ or chronic obstructive pulmonary disease/ or chronic obstructive respiratory disease
15	12 or 13 or 14
16	1 and 11 and 15

Appendix 1j. Search terms for studies on COPD in Africa (Global Health)

#	*Search terms*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp Emphysema/
13	copd.mp.
14	exp chronic obstructive pulmonary disease/ or bronchitis, chronic/ or exp pulmonary emphysema/ or respiratory disease
15	12 or 13 or 14
16	1 and 11 and 15

Appendix 1k. Search terms for studies on asthma in Africa (EMBASE)

#	*Searches*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp asthma/ or wheezing/ or obstructive airway disease/ or respiratory tract allergy/ or allergic asthma/ or aspirin exacerbated respiratory disease/ or asthmatic state/ or exercise induced asthma/ or nocturnal asthma/ or occupational asthma
13	1 and 11 and 12

Appendix 1l. Search terms for studies on asthma in Africa (Global Health)

#	*Searches*
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp asthma/ or asma/ or respiratory diseases/ or bronchial asthma/ or atopy/ or immediate hypersensitivity/ or wheezing
13	1 and 11 and 12

APPENDIX 2. All data points employed in hypertension modelling

Study ID	*Country*	*Author*	*Study year*	*Data type*	*Mean age (all)*	*Cases (All)*	*Sample sizes (All)*	*Prevalence (All)*	*cases (Men)*	*Sample sizes (Men)*	*Prevalence (Men)*	*cases (Women)*	*denominator (Women)*	*Prevalence (Women)*
YEAR 1990														
6	Sudan	Ahmed 1990	1988-89	urban	35	38	510	7.5						
14	Senegal	Astagneau 1992	1989-90	urban	31.45	516	2300	22.5	246	1041	23.6	271	1259	21.5
22	Nigeria	Bunker et al. 1992	1987-88	urban	36.35	174	559	31.1	150	438	34	20	121	17
28	Cameroon	Cruickshank et al. 2001	1991	mixed	41.75	253	3578	7.07098938	136	1524	8.92388451	117	2054	5.69620253
38	Cameroon	Fezeu et al. 2010	1994	mixed	54.5	332	1762	18.8422247	153	757	20.2113606	179	1005	17.8109453
40	Liberia	Giles et al. 1994	1991-92	rural	54.5	449	3588	12.5						
46	Egypt	Ibrahim et al. 1995	1991-93	mixed	45.6	1771	6733	26.3	860	3348	25.7	911	3385	26.9
62	DR Congo	M'Buyamba-Kabangu	1983-84	urban	42.5	71	424	16.7	42	190	22.1	29	234	12.4
83	South Africa	Steyn et al. 1986	1982	mixed	59	407	976	41.6910861	223	490	45.6	183	486	37.75
84	South Africa	Steyn et al. 1996	1990	mixed	40.5	212	986	21.5172414	85	442	19.2	127	544	23.4

YEAR 2000														
16	Guinea	Balde et al. 2006	2003	mixed	62	483	1537	31.4						
19	Tunisia	Ben Romdhane et al. 2005	2002-03	mixed	54.5	814	1837	44.3	291	752	38.7	523	1084	48.2
20	Tanzania	Bovet et al. 2002	1998-99	urban	54.5	2683	9254	28.9910201	978	3609	27.1	1705	5645	30.2
23	Ghana	Burket 2006	2003	rural	53	94	287	32.8						
25	Ghana	Cappuccio et al. 2004	2001	mixed	54.7	291	1013	28.7	115	385	29.9	176	628	28
27	Nigeria	Cooper et al. 1997	Nigeria 1995	mixed	49.5	364	2509	14.5	172	1171	14.7	191	1338	14.3
27	Cameroon	Cooper et al. 1997-a	Cameroon 1995	mixed	49.5	478	2828	16.9	240	1357	17.7	240	1471	16.3
33	Tanzania	Edwards et al. 2000	1996	Ilala rural	39.95	224	767	29.2046936	99	330	30	125	437	28.6
33	Tanzania	Edwards et al. 2000-a	1996	Shari rural	54.5	295	928	31.7887931	129	401	32.2	166	527	31.5
38	Cameroon	Fezeu et al. 2010-a	2003	mixed	54.5	536	1398	38.3404864	249	609	40.8866995	287	789	36.3751584
39	Tunisia	Ghannem & HadjFredj	1995	urban	54.5	277	957	28.9	87	290	30	190	667	28.4

51	Ghana	Koopman et al. 2012	2002-10	rural	66	223	924	24.1623377	123	480	25.7	100	444	22.5
52	Tunisia	Laouani Kechrid et al. 2004	2002-03	mixed	69	416	600	69.3						
59	Madagascar	Mauny et al. 2003	1996-97	urban	32.75	178	773	23.3	90	360	24.9	88	413	21.7
63	Egypt	Mohammed et al. 2000	1999-00	rural	42.5	538	1927	27.9						
67	Guinea	N'Gouin-Claih et al. 2003	2001	rural	45.5	85	188	45.2						
74	Nigeria	Oladapo et al. 2010	2002-05	rural	42.1	415	2000	20.8	184	873	21.1	231	1127	20.5
85	South Africa	Steyn et al. 2004	1996	peri-urban	42	264	974	27.1351129	137	428	31.9	128	546	23.4
89	Morocco	Tazi et al. 2003	2000	mixed	51	713	1802	39.6	281	755	37.2	432	1047	41.3
91	South Africa	Thorogood et al. 2007	2002	rural	59.5	131	402	32.6						
95	Gambia	van der Sande et al. 2000	1998-99	mixed	43.7	992	5389	18.4						
YEAR 2010														
1	Nigeria	Abegunde & Owoaje 2013	2010-11	mixed	71.1	219	630	34.7619048						
2	Ghana	Addo et al. 2006	2004-05	rural	42.4	92	362	25.4	26	107	24.1	66	255	25.9

3	Nigeria	Adedoyin et al. 2008	2007-08	semiurban	44.2	767	2097	36.576061	326	886	36.7945824	441	1212	36.3861386
4	Nigeria	Adedoyin et al. 2012	2011-12	semiurban	41.5	248	1004	25.2	136	550	24.7	112	454	24.7
5	Ghana	Agyemang 2006	2004	mixed	35.9	421	1431	29.4	200	644	31.0447205	221	787	28.0767471
7	Nigeria	Ahaneku et al. 2011	2010-11	rural	57.3	97	218	44.5	34	69	49.3	63	149	42.3
8	South Africa	Alberts et al. 2005	2004-05	rural	59.5	579	2062	28.0626091	122	499	24.5	456	1563	29.2
9	Nigeria	Alikor et al. 2013	2012-13	rural	41.3	101	500	20.2	32	156	20.5	69	344	20.1
10	Tunisia	Allal-Elasmi. 2012	2004-05	mixed	44.6	843	2712	31.0738938	307	1228	25	536	1484	36.1
11	Nigeria	Amira et al. 2012	2006-10	urban	41.9	456	1368	33	276	720	38.3	180	648	27.8
12	Nigeria	Amole et al. 2011	2008	mixed	48.7	202	400	50.5	93	179	52	109	221	49.3
13	Ethiopia	Araya Giday & Tadesse 2011	2008	mixed	36.08	97	979	9.9						
15	Ethiopia	Awoke et al. 2012	2012	urban	51.4	192	679	28.3	84	323	26	108	356	30.3
17	Togo	Baragou et al. 2012	2009-10	urban	39	532	2000	26.6	243	945	25.7	289	1055	27.6
18	Tunisia	Ben Romdhane et al. 2012	2004-05	mixed	49.6	2428	8007	30.6	920	3417	27.3	1508	4590	33.1

21	Seychelles	Bovet et al. 2006	2004	mixed	44.5	397	1255	31.6	241	628	38.4	155	627	24.8
24	Angola	Capingana et al. 2013	2009-10	urban	44.5	278	615	45.2	136	294	46.3	142	321	44.2
26	Ghana	Cook-Huynh et al . 2012	2006-07	rural	53.5	114	326	35	35	94	37.2	79	232	34.1
29	Mozambique	Damasceno et al. 2009	2005	mixed	54.5	1020	3081	33.1	457	1281	35.7	562	1800	31.2
30	Malawi	de Ramirez et al. 2010	2007	rural Malawi	38.4	94	406	23	40	163	25	53	243	22
30	Rwanda	de Ramirez et al. 2011-a	2007	rural Rwanda	42.2	86	535	16	34	216	16	52	319	16
30	Tanzania	de Ramirez et al. 2012-b	2007	rural Tanzania	42.8	145	542	27	93	328	28	52	213	24
31	Tanzania	Dewhurst et al. 2013	2009-2010	rural	76	1553	2223	69.9	605	972	62.2427984	948	1251	75.7793765
32	Chad	Dionadji et al. 2010	2004	rural	35	68	412	16.4	27	222	12.1621622	41	190	21.5789474
34	Nigeria	Ejim et al. 2011	2005-06	rural	59.8	398	858	46.4	124	247	50.2	274	611	44.8
35	Nigeria	Ekanem et al. 2013	2012	semi urban	31.7	201	442	47	129	228	30.1	72	214	16.8
36	Nigeria	Ekwunife et al. 2010	2009	mixed	34.9	160	756	21.1						

41	Zambia	Goma et al. 2011	2009-10	urban	57	658	1928	34.8	337	634	38	419	1288	33.3
42	Algeria	Hamida et al. 2013	2010	rural	58.5	365	722	50.2	123	238	51.3	240	484	49.7
43	Tunisia	Hammami et al. 2011	2008-09	rural	72.3	311	598	52	91	202	45	220	396	55.5
44	Nigeria	Hendriks et al. 2012	2009-11	Nigeria rural	45.3	563	2678	21						
44	Kenya	Hendriks et al. 2012-a	2009-11	Kenya rural	40.9	426	2111	20.2						
44	Tanzania	Hendriks et al. 2012-b	2009-11	Tanzania urban	36.8	199	1046	19						
44	Namibia	Hendriks et al. 2012-c	2009-11	Namibia urban	36.9	555	1733	32						
45	Benin	Houinato et al. 2012	2008	mixed	42.7	1912	6853	27.9						
47	Nigeria	Isezuo et al.2011	2009-10	mixed	38.9	194	782	24.8	106	409	25.9	88	373	23.6
49	Cameroon	Kamadjeu et al. 2006-a	2004	urban Douala	31.35	377	2559	20.8						
50	DR Congo	Katchunga et al. 2011	2009-10	mixed	54.5	281	699	40.2						
53	Algeria	Latifa & Kaouel 2007	2004-05	urban	54.5	263	805	32.7	98	399	24.5	165	406	40.6

55	South Africa	Malaza et a.l 2012	2010	rural	54.5	3090	11786	26.2	728	3500	20.8	2362	8286	28.5
56	Senegal	Macia et al. 2012	2009	urban	69.5	327	500	65.4	168	263	63.9	159	237	67.1
57	Uganda	Maher et al. 2011	2008-09	rural	32.75	1489	6678	22.3	602	2719	22.5	887	3959	22.6
58	Kenya	Mathenge et al. 2010	2007-08	mixed	69.5	2191	4376	50.1						
60	Uganda	Mayega et al. 2012	2011	rural	42.5	340	1656	20.5	167	805	20.7	173	851	20.4
61	Nigeria	Mbah et al. 2013	2011-12	semi-urban	50	65	200	32.5						
64	Malawi	Msyamboza et al. 2012	2009	mixed	45.5	1237	3727	33.2	438	1187	36.9	759	2540	29.9
65	Eritea	Mufunda et al. 2006	2004	mixed	39.5	376	2352	16	196	1160	16.88	181	1182	15.28
66	Uganda	Musinguzi & Nuwaha 2013	2012	mixed	35.15	997	4563	21.8	362	1623	22.3	635	2940	21.7
68	Burkina Faso	Niakara et al. 2007	2004	urban	54.5	839	2087	40.2						
69	Ethiopia	Nshisso et al. 2012	2009	urban	50.5	413	2153	19.1	286	1298	22	127	855	14.9
70	Nigeria	Odugbemi et al. 2012	2009-10	urban	43.885	139	400	34.8						
71	Nigeria	Ogah et al. 2013	2011-12	mixed	41.7	931	2928	31.8	479	1430	33.5	474	1553	30.5

72	Nigeria	Oghagbon et al. 2008	2006-07	urban	50.5	76	281	27.1	60	211	28.4	16	70	22.9
76	Nigeria	Omorogiuwa et al. 2009	2007-08	urban	41.6	396	1200	33	137	488	28.1	259	712	36.4
77	Nigeria	Omuemu et al. 2007	2004-05	rural	30.7	119	590	20.2	88	355	24.8	31	235	13.2
78	South Africa	Peltzer & Phaswana-Mafuya	2008	mixed	65	2842	3840	77.3	1159	1638	74.4	1683	2202	79.6
79	Angola	Pires et al. 2013	2011	mixed	41.5	337	1464	23	158	598	26.4	171	866	19.8
86	Nigeria	Suleiman et al. 2013	2011	semi-urban	50.5	60	400	15	30	160	18.8	30	240	12.5
88	Algeria	Temmar et al. 2007		peri-urban	55	594	1346	44	262	635	41.2598425	332	711	46.6947961
90	Ethiopia	Tesfaye et al. 2009	2006	urban	49.5	982	3273	30.0105408	440	1398	31.5	542	1875	28.9
92	Ethiopia	Tran et al. 2011	2009-2010	urban	42.9	343	1935	17.7494574	234	1171	20	109	764	14.3
93	Nigeria	Ulasi et al. 2010	2007-08	mixed	40.8	478	1458	32.8						
94	Nigeria	Ulasi et al. 2011	2009-10	mixed	38.02	290	688	42.2	164	354	46.3	126	334	37.7
96	Kenya	van de Vijver et al. 2013	2009-09	urban	48.5	638	5190	12.3	355	2794	12.7	288	2396	12
97	Uganda	Wamala et al. 2009	2006	rural	42	252	842	30.4	102	441	25.4	150	401	34

98	Ghana	Williams et al. 2013	2012	rural	53.84	190	425	44.7						
100	Togo	Yayehd et al. 2013	2011	urban	40.8	734	2002	36.7	314	907	34.6	420	1095	38.4

APPENDIX 3. All data points employed in stroke modelling

Study Id	*Author, year*	*Year*	*Age*	*Cases (All)*	*Sample sizes (All)*	*Prevalence (Incidence) /100000 (All)*	*Cases (Men)*	*Sample sizes (Men)*	*Prevalence (Incidence) /100000 (Men)*	*Cases (Women)*	*Sample sizes (Women)*	*Prevalence (Incidence) /100000 (Women)*
PREVALENCE DATA												
1	Connor et al. 2004	2001-02	all 15+	103	42378	243	37	20042	185	66	22336	296
			15-24	2	15358	13						
			25-34	6	10315	58						
			35-44	8	6855	117						
			45-54	21	4340	484						
			55-64	19	2497	761						
			65-74	22	1925	1143						
			75-84	22	901	2442						
			85+	3	187	1604						
3	Cossi et al. 2012	2008-09	all 15+	70	15155	460	38	6293	610	32	8862	360
			15-44	4	12580	30	3	5300	60	1	7279	10
			45-54	17	1212	1400	9	443	2030	8	769	1040

			55-64	19	799	2380	9	309	2910	10	490	2040
			65-74	18	348	5170	10	159	6290	8	189	4230
			75-84	10	134	7460	6	50	12000	4	84	7410
			85+	2	30	6670	1	9	11100	1	21	4760
5	Danesi et al. 2007	2005-06	all 0+	15	13127	114	11	7295	151	4	5832	69
			35-44	1	1802	56	1	999	100	0	803	0
			45-54	3	1219	246	3	704	426	0	515	0
			55-64	4	492	813	1	284	357	3	211	1421
			65-74	3	203	1478	2	120	1667	1	83	1205
			75-84	3	66	4545	3	46	6522	0	20	0
			85+	1	21	4761	1	8	12500	0	13	0
7	Dewhurst et al. 2013	2009-10	70+	51	2232	2300		976			1256	
8	El Tallawy et al. 2013	2009-12	all 20+	130	19848	655	85	9916	860	48	9932	480
			20-39	3	11664	26						
			40-59	49	6077	806						
			60+	78	2107	3702						
12	Farghaly et al. 2013a (El Tallawy 2010)	2005-09	all 0+	351	62583	560	196	32165	610	155	30418	510

	Farghaly et al. 2013b (El Tallawy 2010)	2005-09	all 0+	257	44600	580	142	22908	620	115	21692	530
	Farghaly et al. 2013c (El Tallawy 2010)	2005-09	all 0+	94	17983	520	54	9257	580	40	8726	460
			20-39	18	20334	90						
			40-59	114	11545	990						
			60+	212	3937	5380						
15	Kandil et al. 2006a	1992-93	all 0+	127	25000	508	65		520	62		490
15	Kandil et al. 2006b	1992-93	all 0+	35	8464	410	20		460	15		470
15	Kandil et al. 2006c	1992-93	all 0+	61	11228	540	29		510	32		570
			20-39	17	6629	260						
			40-59	56	4017	1390						
			60+	52	1688	3080						
16	Khedr et al. 2013	2010	0+	57	5920	963	36	3066	1174	21	2854	736
17	Attia Romdhane et al. 1993	1985	0+	15	34874	42						
18	Osuntokun et al. 1987	1982	0+	11	18954	58						

19	Tekle-Haimanot et al. 1990	1988	20-85	9	60820	15						
INCIDENCE DATA												
6i	Danesi et al. 2013	2007	all 0+	189	750000	25.2	118	417000	28.3	71	333000	21.3
			25-34	9	148560	6.1	5	83400	6	4	65160	6.1
			35-44	22	102860	21.4	15	57127	28.8	7	45733	15.3
			45-54	36	69750	51.6	24	40446	59.4	12	29304	40.95
			55-64	54	28610	188.7	36	16262	221.4	18	12348	145.8
			65-74	50	11343	440.8	22	6680	329.3	28	4663	600.5
			75-84	14	3501	399.9	12	2502	479.6	2	999	200.2
			85+	4	1086	368.3	4	418	956.9			
8i	El Tallawy et al. 2013	2012	all 20+	36	19848	181	21	9916	212	15	9932	150
			40-59	16	6077	263						
			60+	20	2107	950						
11i	Walker et al. 2010a	2006	all 0+	453	159814	94.5	235	71916.3	106.7	10	87897.7	76.7
			0-44	34	60216.7	9	17	21948.06	8	17	39132.21	9.9
			45-54	32	38600.72	82.9	20	21905.81	91.3	12	15810.28	75.9
			55-64	55	26712	205.9	30	12484.39	240.3	25	14068.66	177.7

			65-74	116	20415.35	568.2	66	9776.329	675.1	50	10636.03	470.1
			75-84	139	9981.33	1392.6	70	4175.365	1676.5	69	5996.35	1150.7
			85+	77	3887.907	1980.5	32	1626.347	1967.6	45	2254.17	1996.3
11ii	Walker et al. 2010b	2006	all 0+	183	56517	107.9	92	25432.65	115.2	91	31084.35	99.7
			0-44	30	35977.15	20.1	14	11141.5	19.5	16	20470.07	20.8
			45-54	27	11344.54	238	17	9900.99	171.7	20	6172.84	324
			55-64	33	5709.343	578	17	2930.024	580.2	16	2784.061	574.7
			65-74	55	2399.965	2291.7	23	887.1403	2592.6	22	1154.977	1904.8
			75-84	32	840.0053	3809.5	18	431.9965	4166.7	14	400.4004	3496.5
			85+	6	246.0025	2439	3	140.9973	2127.7	3	101.9992	2941.2
12	Farghaly et al. 2013a	2007	52.5	156	62583	250	86	32165	270	70	30418	230
	Farghaly et al. 2013b	2007	48.9	114	44600	260	63	22908	280	51	21692	240
	Farghaly et al. 2013c	2007	54.4	42	17983	230	23	9257	250	19	8726	220
14i	Osuntokun et al. 1979	1975	all 0+	318	1223077	26	229	538461.5	25	89	684615.4	13
			20-29	8	800000	1	5	500000	1	3	300000	1
			30-39	26	236363.6	11	18	150000	12	8	100000	8
			40-49	70	104477.6	67	54	60000	90	16	40000	40
			50-59	80	39603.96	202	55	22000	250	25	17857.14	140

			60-69	87	19772.73	440	60	11111.11	540	27	9310.345	290
			70-79	32	6956.522	460	28	3589.744	780	4	3076.923	130
			80+	10	4761.905	210	5	2500	200	5	2380.952	210
15i	Kandil et al. 2006a	1993	all 0+	39	25000	180	21	21000	100	18	21176.47	85
	Kandil et al. 2006b	1993		11	8464	150	7	7777.778	90	4	7547.17	53
	Kandil et al. 2006c	1993		20	11228	210	9	9278.351	97	11	9243.697	119
			20-39	6	5774	104						
			40-59	12	3073	390						
			60+	19	1302	1460						

APPENDIX 4. All data points employed in diabetes modelling

Study ID	*Country*	*Study period*	*Data type*	*Mean Age*	*Cases (All)*	*Sample size (All)*	*Prevalence (All)*	*Cases (Men)*	*Sample size (Men)*	*Prevalence (Men)*	*Cases (Women)*	*Sample size (Women)*	*Prevalence (Women)*
1	Ghana	2001	Diabetes	44.3	300	3462	6.4	145	1309	11	155	2153	7.2
1	Ghana	2001	IGT	44.3	502	3462	10.7	178	1309	13.6	324	2153	15
1	Ghana	2001	IFG	44.3	289	3462	6	143	1309	10.9	146	2153	6.8
2	Tanzania	1997	ALL	54.5									
2	Tanzania	1997	Diabetes	54.5	47	1698	2.8	24	733	3.3	23	965	2.4
2	Tanzania	1997	IFG	54.5	50	1698	2.9	18	733	2.5	32	965	3.3
			RURAL										
2	Tanzania	1997	Diabetes	54.5	12	928	1.3	6	401	1.5	6	527	1.1
2	Tanzania	1997	IFG	54.5	13	928	1.4	5	401	1.2	8	527	1.5
			URBAN										
2	Tanzania	1997	Diabetes	54.5	35	770	4.5	18	332	5.3	17	438	4
2	Tanzania	1997	IFG	54.5	37	770	4.8	13	332	4	24	438	5.4
3	Guinea	2003	ALL	49.4									
3	Guinea	2003	Diabetes	49.4	94	1537	6.1	45	730	6.2	49	807	6.1

3	Guinea	2003	IFG	49.4	206	1537	13.4						
			RURAL										
3	Guinea	2003	Diabetes	49.4	26	651	4						
3	Guinea	2003	IFG	49.4	91	886	10.3						
			URBAN										
3	Guinea	2003	Diabetes	49.4	68	886	7.7						
3	Guinea	2003	IFG	49.4	115	651	17.7						
4	Sierra Leone	1996	Diabetes (All)	35.7	6	501	1.2	5	247	2	1	254	0.4
4	Sierra Leone	1996	Diabetes (rural)	35.7	0	256	0						
4	Sierra Leone	1996	Diabetes (urban)	35.7	6	245	2.4						
5	South Africa	1993	Diabetes	73.8	51	200	28.7	22	96	25.7	29	104	30.3
5	South Africa	1993	IGT	73.8	24	200	15	17	96	23.7	7	104	9.8
6	Kenya	2008	ALL	38.6									
6	Kenya	2008	Diabetes	38.6	61	1459	4.2	27	615	4.5	34	844	4.2
6	Kenya	2008	IFG	38.6	175	1459	12	37	615	6.1	110	844	13.1
			RURAL										

6	Kenya	2008	Diabetes	38.6	26	1180	2.2						
6	Kenya	2008	IFG	38.6	101	1180	8.6						
			URBAN										
6	Kenya	2008	Diabetes	38.6	34	279	12.2						
6	Kenya	2008	IFG	38.6	37	279	13.2						
7	Ghana	2007	(Rural) Diabetes	52	25	326	7.7						
8	Senegal	2009	(Urban) Diabetes	57	107	600	17.8	43	307	14	64	293	21.8
9	Mauritania	1985	Diabetes	34.6	14	744	1.88	4	307	1.3	10	437	2.29
10	Cameroon	2011	(Urban) Diabetes	43.7	307	2120	14.4	218	1591	13.7	89	529	17
11	Sudan	1995	ALL	59.5									
11	Sudan	1995	Diabetes	59.5	44	1284	3.4	16	461	3.5	28	823	3.4
11	Sudan	1995	IFG	59.5	37	1284	2.9	10	461	2.2	27	823	3.3
			RURAL										
11	Sudan	1995	Diabetes	59.5	12	458	2.62						
11	Sudan	1995	IFG	59.5	10	458	2.18						
			URBAN										
11	Sudan	1995	Diabetes	59.5	32	826	3.87						

11	Sudan	1995	IFG	59.5	27	826	3.27						
12	Nigeria	1988	Diabetes		40	2800	1.43	75	1727	4.3	15	1073	1.4
13	South Africa	1992	(Urban) Diabetes	57	102	563	18.1						
13	South Africa	1992	IFG	57	25	563	4.4						
13	South Africa	1992	IGT	57	86	563	15.3						
14	Morocco	2010	Diabetes (type 1&2)	54.48	234	610	38.6						
15	Angola	2009	(Rural) Diabetes	54.3	12	421	2.8	4	124	3.2	8	297	2.7
15	Angola	2009	IGT	54.3	34	421	8.1	7	124	5.6	27	297	9.1
16	Nigeria	1995	Diabetes	60.8	8	500	1.6	3	205	1.4	5	295	1.9
17	Seychelles	2005	Diabetes	45.2	144	1255	11.5	62	568	11	82	687	12.1
17	Seychelles	2005	IFG	45.2	304	1255	24.2	172	568	30.4	123	687	18
17	Seychelles	2005	IGT	45.2	130	1255	10.4	63	568	11.2	67	687	9.6

18	South Africa	2007	Diabetes	46	42	552	7.6	8	155	5.2	34	397	8.6
18	South Africa	2007	IFG	46	35	552	6.3	7	155	4.5	28	397	7.1
19	Zimbabwe	2005	Diabetes	59.7	115	3081	3.7	32	770	4.2	83	2311	3.4
20	Egypt	1994	Diabetes (All)	59.7	429	4620	9.3						
20	Egypt	1994	Diabetes (Rural)	59.7	79	1619	4.9						
20	Egypt	1994	Diabetes (Urban)	59.7	350	3001	11.7						
21	South Africa	1990	Diabetes	56	46	717	6.3	14	214	6.5	32	503	6.4
21	South Africa	1990	IGT	56	43	717	5.9	13	214	6	30	503	5.9
22	Uganda	2009	(Rural) Diabetes	48	23	5719	0.4	10	2307	0.4	13	3412	0.4
22	Uganda	2009	IGT	48	172	5719	3	74	2307	3.2	98	3412	2.9
			ALL										
23	Cameroon	1995	Diabetes	49	18	1767	1.02	7	750	0.9	11	1017	1.1
23	Cameroon	1995	IGT	49	46	1767	2.6	25	750	3.3	21	1017	2.1
			RURAL										

23	Cameroon	1995	Diabetes	49	5	719	0.7	3	292	0.9	2	427	0.5
23	Cameroon	1995	IGT	49	16	719	2.2	17	292	5.8	9	427	2.2
			URBAN										
23	Cameroon	1995	Diabetes	49	13	1048	1.2	4	458	0.8	9	590	1.6
23	Cameroon	1995	IGT	49	20	1048	1.9	8	458	1.8	12	590	2
24	Tanzania	1987	(Rural) Diabetes	37	53	6087	0.87	29	2627	1.1	24	3460	0.68
24	Tanzania	1987	IGT	37	468	6087	0.8	192	2627	6.9	276	3460	7.7
25	South Africa	2003	(Rural) Diabetes	46.9	46	999	4.6	9	200	4.5	37	799	4.6
25	South Africa	2003	IGT	46.9	64	999	6.4	13	200	6.5	51	799	6.4
25	South Africa	2003	IFG	46.9	16	999	1.6	9	200	4.5	7	799	0.9
26	Tanzania	2007	(Urban) Diabetes	59.7	13	209	6						
27	Zambia	2007	(Urban) Diabetes	59.7	75	1478	5.1	21	495	4.2	54	983	5.5
28	Ethiopia	2010	Diabetes	57	140	2153	6.5	83	1298	6.4	57	855	6.6

28	Ethiopia	2010	IGT	57	465	2153	21.6	288	1298	22.2	187	855	21.8
29	Nigeria	2000	Diabetes	48.9	34	502	6.8	21	273	7.7	13	299	5.7
30	Nigeria	2011	(Urban) Diabetes	49	14	301	4.7	6	112	2	8	189	2.7
30	Nigeria	2011	IFG	49	10	301	3.3	5	112	1.65	5	189	1.65
31	Nigeria	2005	(Rural) Diabetes	42.1	49	2000	2.5	18	873	2.1	31	1127	2.8
32	Nigeria	1995	(Urban) Diabetes	40.8	7	849	0.8	4	487	0.82	3	362	0.83
32	Nigeria	1995	IGT	40.8	19	849	2.2	11	487	2.26	8	362	2.21
33	Congo DR	2005	Diabetes	46	2600	9770	10						
33	Congo DR	2005	IFG	46	1030	9770	8.3						
33	Congo DR	2005	IGT	46	670	9770	26.6						
34	Tunisia	1987	Diabetes (All)	57	168	5613	2.99	87	2381	3.65	81	3232	2.51
			Diabetes (Rural)		24	1787	1.34	18	792	2.3	6	995	0.6
			Diabetes (Urban)		144	3826	3.76	69	1589	4.3	75	2237	3.4
35	South Africa	2009	(Urban) Diabetes	43.3	160	1071	14.9	64	509	12.6	96	562	17.1

35	South Africa	2009	IGT	43.3	125	1071	11.7	60	509	11.8	65	562	11.6
35	South Africa	2009	IFG	43.3	14	1071	1.3	8	509	1.6	6	562	1.1
			ALL										
36	Mozambique	2005	Diabetes	44.5	82	2343	3.5	23	942	2.5	59	1401	4.2
36	Mozambique	2005	IFG	44.5	58	2343	2.5	18	942	1.9	40	1401	2.9
			RURAL										
36	Mozambique	2005	Diabetes	44.5	19	1125	1.7	5	442	2.4	14	683	1.2
36	Mozambique	2005	IFG	44.5	28	1125	2.5	2	442	2.3	26	683	2.6
			URBAN										
36	Mozambique	2005	Diabetes	44.5	63	1218	5.2	18	500	5.5	45	718	4.9
36	Mozambique	2005	IFG	44.5	30	1218	2.5	16	500	3.2	14	718	2
			1987										
37	Mauritius	1987	Diabetes	43.1	696	4991	12.8	334	2339	13	362	2652	12.6
37	Mauritius	1987	IGT	43.1	823	4991	16.1	308	2339	12.7	515	2652	19.1

37	Mauritius	1987	IFG	43.1	192	4991	3.8	120	2339	5.1	72	2652	2.6
			1992										
37	Mauritius	1992	Diabetes	45.2	1213	6463	15.2	577	2986	15.5	636	3477	15
37	Mauritius	1992	IGT	45.2	1003	6463	14.3	389	2986	12	614	3477	16.3
37	Mauritius	1992	IFG	45.2	399	6463	5.9	255	2986	8.2	144	3477	3.9
			1998										
37	Mauritius	1998	Diabetes	48.6	1317	5392	17.9	602	2392	18.3	715	3000	17.6
37	Mauritius	1998	IGT	48.6	831	5392	14	316	2392	11.2	515	3000	16.2
37	Mauritius	1998	IFG	48.6	241	5392	4.3	137	2392	6.2	104	3000	2.9
38	Morocco	2000	Diabetes (All)	57	151	1802	8.4	65	755	8.6	86	1047	8.2
38	Morocco	2000	Diabetes (Rural)	57	54	950	5.6						
38	Morocco	2000	Diabetes (Urban)	57	97	852	11.3						
39	Ghana	2010	Diabetes	55	23	597	3.85	10	288	3.5	13	309	4.2
40	Tanzania	1983	Diabetes (All)	57	50	3145	1.6						
			Diabetes (Rural)		5	1003	0.5						

			Diabetes (Urban)		45	2142	1.9						
41	Nigeria	2007	(Urban) Diabetes	59.4	4	199	2						
41	Nigeria	2007	IFG	59.4	5	199	2.5						
42	Chad	2004	(Rural)Diabetes	59.4	29	412	7.4	8	222	2.8	19	190	9
43	Benin	2011	(Urban) Diabetes	59.4	77	1673	4.6	28	534	4.7	49	1039	4.5
43	Benin	2011	IFG	59.4	58	1673	3.5						
44	Sudan	1997	Diabetes	59.4	60	724	8.3	28	282	9.9	32	442	7.5
44	Sudan	1997	IFG	59.4	57	724	7.9	16	282	4.1	41	442	9.7
45	South Africa	2000	(Urban) Diabetes	67	9	374	2.45	4	170	2.4	5	204	2.5
45	South Africa	2000	IFG	67	10	374	2.7	6	170	3.4	4	204	1.5
46	Mali	1987	Diabetes	59.4	69	7472	0.92						
47	Tunisia	2001	Diabetes (All)	42.5	49	692	7.2	21	318	6.6	28	374	7.5
47	Tunisia	2001	Diabetes (Rural)	42.5	9	281	3.25	3	150	2	6	131	4.5
47	Tunisia	2001	DiabEtes (Urban)	42.5	40	411	9.8	18	199	9.2	22	212	10.4
48	Tunisia	1981	Diabetes		223	9712	2.3						
49	Libya	2000	(Urban) Diabetes	57	122	868	14.1	51	314	16.3	71	554	13
49	Libya	2000	IGT	57	74	868	8.5	27	314	8.6	47	554	8.5

50	Algeria	2000	Diabetes	47	119	1457	8.2						
50	Algeria	2000	IGT	47	103	1457	7.1						
51	Nigeria	1995	Diabetes	62	7	247	2.8						
52	Algeria	2006	Diabetes (All)	59.5	1087	7656	14.2	501	2455	20.4	586	5201	10.7
52	Algeria	2006	Diabetes (Rural)	59.5	214	1660	12.9						
52	Algeria	2006	Diabtes (Urban)	59.5	873	5996	15.3						

APPENDIX 5. All data points employed in asthma modelling

Study ID	*Author*	*Country*	*Year*	*Mean age*	*Cases (All)*	*Sample size (All)*	*Prevalence % (All)*	*Cases (Male)*	*Sample size (Male)*	*Prevalence % (Male)*	*Cases (Female)*	*Sample size (Female)*	*Prevalence % (Female)*
wheeze @ rest (12mth)													
1	Ait-Khaled et al. 2007	Algeria	2003	13.5	367	4312	8.7						
1	Ait-Khaled et al. 2007	Cameroon	2003	13.5	169	3066	5.7						
1	Ait-Khaled et al. 2007	Congo Braz	2003	13.5	201	1010	19.9						
1	Ait-Khaled et al. 2007	Cote d'ivoire	2003	13.5	645	3312	19.3						
1	Ait-Khaled et al. 2007	Gabon	2003	13.5	324	3166	10.2						
1	Ait-Khaled et al. 2007	Morocco	2003	13.5	285	1769	16						
1	Ait-Khaled et al. 2007	DR Congo	2003	13.5	221	2950	7.5						
1	Ait-Khaled et al. 2007	Guinea	2003	13.5	578	3138	18.6						
1	Ait-Khaled et al. 2007	Sudan	2003	13.5	361	2909	12.5						
1	Ait-Khaled et al. 2007	Togo	2003	13.5	520	3095	16.8						
1	Ait-Khaled et al. 2007	Tunisia	2003	13.5	944	6115	15.4						
1	Ait-Khaled et al. 2007	Ethiopia	2003	13.5	290	3142	9.1						
1	Ait-Khaled et al. 2007	Kenya	2003	13.5	543	3036	18						
1	Ait-Khaled et al. 2007	Nigeria	2003	13.5	408	3122	13						

1	Ait-Khaled et al. 2007	South Africa	2003	13.5	1025	5037	20.3	396	2025	19.6	626	2994	20.9
2	Zar et al. 2007	Ethiopia	1995	13.5	371	5978	6.2						
2	Zar et al. 2007	Kenya	1995	13.5	871	6267	13.9						
2	Zar et al. 2007	Nigeria	1995	13.5	327	3057	10.7						
2	Zar et al. 2007	South Africa	1995	13.5	832	5178	16.1	324	2088	15.5	505	3073	16.4
12	Esamai & Anabwani 2002	Kenya	2001	13.5	449	3258	13.8						
15	Dagoye at al. 2004	Ethiopia	2003	3	246	7155	3.4	137	3532	3	109	3623	3.9
17	Ehrlich et al. 1995	South Africa	1994	10.5	509	1899	26.8						
18	Ehrlich et al. 2005	South Africa	1996	29	2253	13826	16.3	817	5671	14.4	1436	8155	17.6
20	Erharbor et al. 2006	Nigeria	2005	25	81	903	9						
22	Khaldi et al. 2005	Tunisia	2004	13.5	442	3350	13.2						
23	Koffi et al. 2000	Cote d'ivoire	1998	13.5	475	3045	15.6						
27*+	Falade et al. 2004	Nigeria	1995	6.5	87	1704	5.1	50	797	6.3	37	907	4.1
28*+	Faniran et al. 1999	Nigeria	1998	9.5	58	566	10.2						
29	Georgy et al. 2006	Egypt	2005	13	379	2570	14.7						
30	Hailu et al. 2003	Ethiopia	1997	13.5	545	3365	16.2						
40	Nyembue et al. 2012	DR Congo	2010	44	217	1412	15.4						
44	Wichmann et al. 2007	South Africa	2005	13.5	742	3926	18.9						
47	Nriagu et al. 1999	South Africa	1998	35.5	253	1060	23.9						

49	Odhiambo et al. 1998	Kenya	1993	10.8	54	568	9.5	34	282	12.1	20	286	7
50	Poyser et al. 2002	South Africa	2000	13.5	750	4688	16						
51	Walraven et al. 2001	Gambia	1997	29.5	196	5399	3.63	64	2149	3	126	3074	4.1
9	Desalu et al. 2009	Nigeria	2006	32	103	810	12.7						
25	Mavale-Manuel et al. 2006	Mozambique	2005	13.5	215	1614	13.3						
Asthma ever (not used in modelling, only included for comparisons)													
2	Zar et al. 2007	Ethiopia	1995	13.5	149	5978	2.5						
2	Zar et al. 2007	Kenya	1995	13.5	702	6267	11.2						
2	Zar et al. 2007	Nigeria	1995	13.5	562	3057	18.4						
2	Zar et al. 2007	South Afr	1995	13.5	678	5178	13.1	292	2088	14	396	3073	12.8
3*	Aguwa et al. 2007	Nigeria	2006	45	38	591	6.5						
5	Bennis et al. 1992	Morocco	1991	10.5	50	1464	3.4						
7	Bezzaoucha 1992	Algeria	1991	18	159	4677	3.42						
8	Benarab-Boucherit et al. 2011	Algeria	2010	11	19	286	6.7						
9	Desalu et al. 2009	Nigeria	2006	32	123	810	15.2	82	385	21.2	41	425	9.6
10	Ehrlich et al. 1998	South Africa	1997	9	1036	1955	53						
11	Esamai & Anabwani 1996	Kenya	1995	13.5	175	3018	5.8						
12	Esamai & Anabwani 2002	Kenya	2001	13.5	410	3258	12.6						

17	Ehrlich et al. 1995	South Africa	1994	12	205	1905	10.8						
18	Ehrlich et al. 2005	South Africa	1996	29	525	13826	3.8	212	5671	3.7	313	8155	3.8
19	Nafti et al. 2009	Algeria	2008	14.1	236	10015	3.45						
19	Nafti et al. 2009	Morocco	2008	14.5	310	10051	3.89						
19	Nafti et al. 2009	Tunisia	2008	13.8	326	10284	3.53						
20	Erharbor et al. 2006	Nigeria	2005	25	127	903	14.1	49	469	10.4	78	434	17.9
24*	Laraqui Hosni et al. 2002	Morocco	2001	37	29	353	8.2						
26	Miningou et al. 2002	Burkina Faso	1998	39.5	78	808	9.6						
27*+	Falade et al. 2004	Nigeria	1995	6.5	52	1704	3.1	32	797	4	20	907	2.2
28*+	Faniran et al. 1999	Nigeria	1998	9.5	34	566	6						
29	Georgy et al. 2006	Egypt	2005	13	246	2609	26.5						
30	Hailu et al. 2003	Ethiopia	1997	13.5	74	3365	2.2						
34	Mengesha & Bekele 1998	Ethiopia	1997	39	69	422	16.3						
35	Miszkurka et al. 2012	Burkina Faso	2001	36	559	4822	11.6						
36	de Almeida et al. 2001	Cape Verde	1993	8	41	588	7						
37	Mustapha et al. 2011	Nigeria	2004	10.5	76	1397	5.4						
39	Musafiri et al. 2011	Rwanda	2009	38.3	163	1920	8.9						
41	Roudaut et al. 1992	Cote d'Ivoire	1990	13	263	2433	10.8						
45	Wolff et al. 2012	Madagascar	2010	10.5	111	1236	9						

47	Nriagu et al. 1999	South Africa	1998	35.5	119	1060	11.2						
49	Odhiambo et al. 1998	Kenya	1993	10.8	25	1172	2.1	14	571	2.5	11	601	1.8
50	Poyser et al. 2002	South Africa	2000	13.5	626	4706	13.3						
51	Walraven et al. 2001	Gambia	1997	32	101	5399	1.87						
52	Yemaneberhan et al. 1997	Ethiopia	1996	23	393	12876	3.05						

APPENDIX 6. Publications from this thesis

Adeloye, D. & Basquill, C. 2014. Estimating the Prevalence and Awareness Rates of Hypertension in Africa: A Systematic Analysis. PLoS One 9(8): e104300. doi:10.1371/journal.pone.0104300

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Estimating the Prevalence and Awareness Rates of Hypertension in Africa: A Systematic Analysis

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Abstract

Background: The burden of hypertension is high in Africa, and due to rapid population growth and ageing, the exact burden on the continent is still far from being known. We aimed to estimate the prevalence and awareness rates of hypertension in Africa based on the cut off "≥140/90 mm Hg".

Methods: We conducted a systematic search of Medline, EMBASE and Global Health. Search date was set from January 1980 to December 2013. We included population-based studies on hypertension, conducted among people aged ≥15 years and providing numerical estimates on the prevalence of hypertension in Africa. Overall pooled prevalence of hypertension in mixed, rural and urban settings in Africa were estimated from reported crude prevalence rates. A meta-regression epidemiological modelling, using United Nations population demographics for the years 1990, 2000, 2010 and 2030, was applied to determine the prevalence rates and number of cases of hypertension in Africa separately for these four years.

Results: Our search returned 7680 publications, 92 of which met the selection criteria. The overall pooled prevalence of hypertension in Africa was 19.7% in 1990, 27.4% in 2000 and 30.8% in 2010, each with a pooled awareness rate (expressed as percentage of hypertensive cases) of 16.9%, 29.2% and 33.7%, respectively. From the modelling, over 54.6 million cases of hypertension were estimated in 1990, 92.3 million cases in 2000, 130.2 million cases in 2010, and a projected increase to 216.8 million cases of hypertension by 2030; each with an age-adjusted prevalence of 19.1% (13.9, 25.5), 24.3% (23.3, 31.6), 25.9% (23.5, 34.0), and 25.3% (24.3, 39.7), respectively.

Conclusion: Our findings suggest the prevalence of hypertension is increasing in Africa, and many hypertensive individuals are not aware of their condition. We hope this research will prompt appropriate policy response towards improving the awareness, control and overall management of hypertension in Africa.

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Introduction

Hypertension and other cardiovascular diseases rank among the leading causes of disabilities and deaths from non-communicable diseases (NCDs) in Africa [1,2], with rising prevalence and death rates now observed more in young and active adults [3]. Recently, the African Union (AU) reported that hypertension is one of the greatest health challenges after HIV/AIDS in the continent [4]. This is in fact a priority globally as conclusions from the 2011 United Nations high level meeting on NCDs focus on a reduction of hypertension and other NCDs, especially in Africa, where the burden is rising at a faster rate compared to other parts of the world [5]. Worldwide, cardiovascular diseases account for about 17 million deaths, with complications from poorly controlled hypertension resulting in over 7.5 million deaths and 57 million disability adjusted life years (DALYS) [6].

The relatively higher prevalence of hypertension in Africa has been linked to population growth and ageing, rising urbanization, mass migration from rural to urban areas, and an increased uptake of western lifestyles including tobacco and alcohol consumption [3,7]. Public health response from the governments of many African nations still remains low, as research findings show that a high number of hypertensive individuals are currently unaware of their condition [8]. Many African countries are yet to implement high blood pressure awareness and control programmes on a population-wide scale, even to people with very high risk of cardiovascular complications [9]. Even with a widely popularised availability of hypertension treatments in some African countries [10], reports show that many rural dwellers are still faced with lack of antihypertensive medications and poor management of cases of hypertension [11]. The WHO has recommended a need for strong public health policies, multisectoral approach, and available and affordable treatment options toward reducing this growing burden of hypertension in Africa [2].

Despite reports of a higher prevalence of hypertension in Africa compared to other world regions [2], public health experts believe the real burden is still far from being known [12]. Many studies in the 1980s and early 1990s were based on the old definition of hypertension (≥160/95 mm Hg) [8,12]. These surveys may possibly underestimate the prevalence of hypertension in Africa in comparison to newer surveys based on ≥140/90 mm Hg.

Moreover, even within studies based on similar case definitions, the variations in reported estimates still suggest the need for more systematic and accurate estimates from larger number of studies towards appropriately informing health service planning and a better response to hypertension in Africa. For example, the World Health Organization (WHO) reported that the prevalence of hypertension in the African region was highest globally in 2008, with an estimated prevalence of 46% [13]. This, though vital for instituting relevant public health response in the continent, elucidates a conflicting state of data in comparison to other hypertension prevalence estimates in Africa which are relatively lower [14,15]. Thus, with an increased research output on hypertension in Africa in the last two decades, a systematic review of population-based studies was conducted towards providing an improved continent-wide estimate of the prevalence and awareness rate of hypertension in Africa, which hopefully may encourage healthy public health policy for a value-added management of hypertension in the region.

Methods

Search strategy

After identifying Medical Subject Headings (MESH) and keywords, a final search strategy was developed. Searches were conducted on three main databases: Medline, EMBASE and Global Health. The search date was set from January 1980 to December 2013. African countries were as listed on the World Bank list of economies (July 2012) [16]. See **Table 1** for details of the search terms.

Selection criteria and case definitions

Cross-sectional population- and/or community-based studies on hypertension were included, published on or after 1980, conducted among people aged ≥15 years, and providing numerical estimates on the prevalence of hypertension in Africa. Studies conducted before 1980, hospital-based, without numerical estimates, on non-human subjects, and that were mainly reviews were all excluded. There were no language restrictions.

Case definitions of hypertension across retained studies comply with the following:

i. systolic blood pressure (≥140 mm Hg) and/or diastolic blood pressure (≥90 mm Hg) and/or self-reported use of antihypertensive medications;

ii. the sixth and seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 6 & 7) [17,18]; and

iii. the 1999 and 2003 World Health Organization/International Society of Hypertension (WHO/ISH) definitions and classification of blood pressure levels [19]

See **Table 2** for details. For the definition of the awareness rate of hypertension in this study, we included studies estimating the prevalence of hypertension based on the definitions above, with awareness rate also being estimated among all identified cases of hypertension and defined as self-report by respondents of any prior diagnosis of hypertension by a doctor or certified health care professional, and excluding women diagnosed during pregnancy, as described by the WHO [19].

Quality criteria

Studies retained were assessed for the following quality:

i. *Study design*: Under this, flaws in the design and execution of study were examined. Basically, this assesses methods of estimation of sample size and sampling methods across studies, and the methods of dealing with design specific issues such as: training of study investigators, adherence to

Table 1. Search terms.

#	Search terms
1	africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	cardiovascular diseases/ or heart diseases/ or exp hypertension/ or peripheral vascular diseases/
13	Hypertensive heart disease.mp. [mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
14	12 or 13
15	1 and 11 and 14
16	limit 15 to (humans and yr = "1980 -Current")

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Table 2. Classification of blood pressure for adults.

Category	JNC				WHO/ISH				
	6		7		1999		2003		
	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	
Optimal	<120	and <80	-	-	<120	<80	-	-	
Normal	120–129	and 80–84	<120	and <80	<130	<85	-	-	
Borderline (JNC)/or High Normal (WHO/ISH)	130–139	or 85–89	120–139 (Pre-hypertension)	or 80–89 (Pre-hypertension)	130–139	85–89	-	-	
Hypertension (JNC),Grade 1 (WHO/ISH)	≥140	or ≥90	≥140	or ≥90	140–159	90–99	140–159	90–99	
Stage 1 (JNC)/or Subgroup Borderline (WHO/ISH)	140–159	or 90–99	140–159	or 90–99	140–149	90–94	-	-	
Stage 2 (JNC)/or Grade 2 (WHO/ISH)	160–179	or 100–109	≥160 (Stage 2)	or ≥100 (Stage 2)	160–179	100–109	160–179	100–109	
Stage 3 (JNC)/or Grade 3 (WHO/ISH)	≥180	or ≥110	-	-	≥180	≥110	≥180	≥110	

JNC Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure; WHO/ISH: World Health Organization/International Society of Hypertension, SBP: systolic blood pressure, DBP: diastolic blood pressure.

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standardized protocol for blood pressure measurement, pre-testing and reviewing questionnaires before data entry, and addressing recall and interviewer's bias appropriately;

ii. *Study analysis*: This assessed the appropriateness of statistical and analytical methods employed across studies in the estimation of hypertension prevalence;

iii. *Generalizability to the African population*: This broadly assessed if the sample size was representative of a larger population that can be generalized to the total African population

An adaptation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines was applied in the final quality grading of studies [20]. See **Box S1**, **Table S1** and **Table S2** in **File S1** for details.

Data extraction and analysis

All extracted data were stored in Microsoft Excel file format. A parallel search and double extraction were conducted by the authors. Data were abstracted systematically on sample size, mean age or age range, number of hypertension cases, and the respective age- and sex-specific prevalence rates. These were sorted into mixed, urban and rural settings (based on studies that reported them). For studies conducted on the same study site, population or cohort, the first chronologically published study was retained, and all additional data from other studies were included in the selected paper.

From all studies, reported crude prevalence rates of hypertension (all expressed as percentages) were pooled, and reported separately for north Africa and sub-Saharan Africa (central, east, south and west), and with rates for urban and rural settings estimated. These were further categorized into 1990, 2000 and 2010, as obtained from studies conducted before 1995, from 1995 to 2004, from 2005 to 2013, respectively. As noted above, awareness rate of hypertension was estimated as number of people who reported being hypertensive, expressed as a percentage of total number of people in the study population having hypertension. Pooled awareness rates of hypertension for 1990, 2000, and 2010, and rates across mixed, urban and rural settings were estimated, respectively.

Description of the modelling

For the modelling and estimation of the total cases of hypertension in Africa, a meta-regression epidemiological model was developed, and applied on crude prevalence rates, sample sizes and respective mean age from all data points. In this model, all data points (mainly the crude prevalence rates and mean age) were plotted on a graph on Microsoft Excel, with all extracted crude prevalence rates plotted on the *y*-axis, i.e. dependent variable, and mean ages corresponding to each prevalence rate are plotted on the *x*-axis, i.e. independent variable. To account for variation in sample sizes from each data point, bubbles were generated on the graph, with the size of each bubble corresponding to the respective sample size reported. Although, it is well known that the prevalence of hypertension in the population significantly increases with age [21], the relationship between age and the disease may not be necessarily linear. Therefore, we experimented with the models based on linear, logarithmic, exponential, Poisson, polynomial, power function and moving average statistical analyses, respectively, and chose the one which was the most predictive, i.e. in which the proportion of variance (R^2) of the disease prevalence explained by age was the greatest. On the model therefore, the fitted curve explaining the largest proportion of variance (best fit) was applied. The equation

generated from the fitted curve was then used to determine the prevalence of hypertension in Africa at midpoints of the United Nations (UN) population 5-year age-group population estimates for Africa, for the years 1990, 2000, 2010, respectively [22], while an overall model was developed from all data points (1980–2013) and used to predict the number of hypertension cases and prevalence rates for 2030. All statistical analyses were conducted on Microsoft Excel and Stata 13.1 (Copyright 1985–2013 Stata Corp LP).

Results

Systematic review

The search returned 7680 publications: Medline (2205), EMBASE (4073) and Global Health (1402). An additional 3 studies were included from other sources (Google Scholar and reference list of relevant reviews). After excluding duplicates, 5227 studies remained. On screening titles for relevance (hypertension studies conducted primarily in an African population setting), 4936 articles were excluded, giving a total of 291 full texts that were assessed. 82 articles did not report hypertension prevalence or population denominators from which prevalence rates can be calculated, 75 articles did not specify study designs and/or clarify case definitions of hypertension, and 42 articles were based on blood pressures base-line of 160/90 mm Hg. A total of 92 studies were finally retained for qualitative synthesis and quantitative analysis (**Figure 1**).

Study characteristics

There were 92 studies conducted across 101 study sites in 31 African countries. Central Africa had 10 study sites, Eastern Africa 21, Northern Africa 12, Southern Africa 15, and Western Africa 43. Nigeria had the highest number of publications with 26 study sites; Ghana and South Africa follow with 7 study sites each, while Cameroon, Tanzania and Tunisia had 6 study sites each (see **Tables 3 and 4**).

73% of studies were completed within a one year, with over 50% carried out in urban settings. The overall sample size from all retained studies was 197734, with a mean and median of 1958 and 1200 respectively. From all studies, the weighted mean systolic and

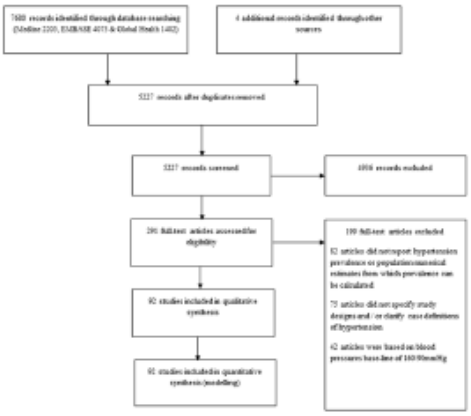

Figure 1. Flow diagram of search results.
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Table 3. Study distribution.

Country	Study sites
Central	
Cameroon	6
Chad	1
DR Congo	2
Rwanda	1
East	
Eritrea	1
Ethiopia	5
Kenya	3
Seychelles	1
Sudan	1
Tanzania	6
Uganda	4
North	
Algeria	3
Egypt	2
Morocco	1
Tunisia	6
South	
Angola	2
Madagascar	1
Malawi	2
Mozambique	1
Namibia	1
South Africa	7
Zambia	1
West	
Benin	1
Burkina Faso	1
Gambia	1
Ghana	7
Guinea	2
Liberia	1
Nigeria	26
Senegal	2
Togo	2
Duration of study	
<1 year	74
1–3 years	22
>3 years	5
Sample size	
<1000	54
1001–3000	37
>3000	10
Study setting	
Rural	47
Urban	50
Mixed (sites overlap with urban and rural)	33

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Table 4. Summary of data from all studies.

Country, Setting	Study period	Diagnostic criteria	Mean age (years)	Prevalence % (all)	Prevalence % (men)	Prevalence % (women)
CENTRAL						
Cameroon, Mixed [44]	1995	≥140/90 mmHg	49.5	16.9	17.7	16.3
Cameroon, Mixed [45]	1991	≥140/90 mmHg	41.75	7.07	8.92	5.69
Cameroon, Mixed [46]	1994	≥140/90 mmHg	54.5	18.8	20.2	17.8
Cameroon, Mixed [46]	2003	WHO/ISH 1999	54.5	38.34	40.9	36.5
Cameroon, Urban) [47]	2003	WHO/ISH 1999	31.35	24.6	25.6	23.1
Cameroon, Urban [47]	2004	WHO/ISH 1999	31.35	20.8	-	-
Chad, Rural [48]	2004	WHO/ISH 2003	35	16.4	12.2	21.8
DR Congo, Mixed [49]	2009–10	WHO/ISH 2003	54.5	40.2	-	-
DR Congo, Urban [50]	1983–84	≥140/90 mmHg	42.5	16.7	22.1	12.4
Rwanda, Rural [51]	2007	JNC 7	42.2	16.0	16.0	16.0
EAST						
Eritea, Mixed [52]	2004	≥140/90 mmHg	39.5	16.0	16.88	15.28
Ethiopia, Mixed [28]	2008	JNC 7, WHO/ISH 2003	36.08	9.9	-	-
Ethiopia, Urban [53]	2012	JNC 7	51.4	28.3	26	30.3
Ethiopia, Urban [54]	2009	≥140/90 mmHg	50.5	19.1	22	14.9
Ethiopia, Urban [55]	2006	≥140/90 mmHg	49.5	30.0	31.5	28.9
Ethiopia, Urban [56]	2009–2010	JNC 7	42.9	17.7	20.0	14.3
Kenya, Rural [57]	2009–11	WHO/ISH 2003	40.9	20.2	-	-
Kenya, Mixed [58]	2007–08	≥140/90 mmHg	69.5	50.1	-	-
Kenya, Urban [59]	2009–09	≥140/90 mmHg	48.5	12.3	12.7	12
Seychelles, Mixed [60]	2004	≥140/90 mmHg	44.5	31.6	38.4	24.8
Sudan, Urban [27]	1988–89	≥140/90 mmHg	35	7.5	-	-
Tanzania, Urban [61]	1998–99	WHO/ISH 1999	54.5	28.9	27.1	30.2
Tanzania, Rural [51]	2007	JNC 7	42.8	27	28	24
Tanzania, Rural [24]	2009–2010	WHO/ISH 2003	76	69.9	62.2	75.8
Tanzania, Rural [62]	1996	WHO/ISH 1999	39.95	29.2	30	28.6
Tanzania, Rural	1996	≥140/90 mmHg	54.5	31.9	32.2	31.5
Tanzania, Urban [57]	2009–11	WHO/ISH 2003	36.8	19	-	-
Uganda, Rural [63]	2008–09	≥140/90 mmHg	32.75	22.3	22.5	22.6
Uganda, Rural [64]	2011	≥140/90 mmHg	42.5	20.5	20.7	20.4
Uganda, Mixed [65]	2012	≥140/90 mmHg	35.15	21.8	22.3	21.7
Uganda, Rural [66]	2006	≥140/90 mmHg	42	30.4	25.4	34
NORTH						
Algeria, Rural) [67]	2010	WHO/ISH 2003	58.5	50.2	51.3	49.7
Algeria, Urban [68]	2004–05	≥140/90 mmHg	54.5	32.7	24.5	40.6
Algeria, Peri-urban [69]	2006–07	≥140/90 mmHg	55	44	41.2	46.7
Egypt, Mixed [70]	1991–93	≥140/90 mmHg	45.6	26.3	25.7	26.9
Egypt, Rural [71]	1999–00	≥140/90 mmHg	42.5	27.9	-	-
Morocco, Mixed [72]	2000	≥140/90 mmHg	51	39.6	37.2	41.3
Tunisia, Mixed [73]	2004–05	JNC 7	44.6	31.07	25.0	36.1
Tunisia, Mixed [74]	2004–05	≥140/90 mmHg	49.6	30.6	27.3	33.1
Tunisia, Mixed [75]	2002–03	≥140/90 mmHg	54.5	44.3	38.7	48.2
Tunisia, Urban [76]	1995	≥140/90 mmHg	54.5	28.9	30	28.4
Tunisia, Rural [77]	2008–09	WHO/ISH 2003	72.3	52	45	55.5-
Tunisia, Mixed [25]	2002–03	≥140/90 mmHg	69	69.3	-	-
SOUTH						
Angola, Urban [78]	2009–10	JNC 7	44.5	45.2	46.3	44.2
Angola, Mixed [79]	2011	≥140/90 mmHg	41.5	23	26.4	19.8

Table 4. Cont.

Country, Setting	Study period	Diagnostic criteria	Mean age (years)	Prevalence % (all)	Prevalence % (men)	Prevalence % (women)
Madagascar, Urban [80]	1996–97	≥140/90 mmHg	32.75	23.3	24.9	21.7
Malawi, Rural [51]	2007	JNC 7	38.4	23	24.5	22
Malawi, Mixed [81]	2009	≥140/90 mmHg	45.5	33.2	36.9	29.9
Mozambique, Mixed [82]	2005	WHO/ISH 1999	54.5	33.1	35.7	31.2
Namibia, Urban [57]	2009–11	WHO/ISH 2003	36.9	32	-	-
South Africa, Rural [83]	2004–05	≥140/90 mmHg	59.5	28.0	24.5	29.2
South Africa, Rural [84]	2010	≥140/90 mmHg	54.5	26.2	20.8	28.5
South Africa, Mixed [23]	2008	≥140/90 mmHg	65	77.3	74.4	79.6
South Africa, Mixed [85]	1982	≥140/90 mmHg	41	41.6	45.6	37.75
South Africa, Mixed [86]	1990	≥140/90 mmHg	40.5	21.5	19.2	23.4
South Africa, Peri-urban [87]	1996	≥140/90 mmHg	42	27.1	31.9	23.4
South Africa, Rural [88]	2002	JNC 7	59.5	32.6	-	-
Zambia, Urban [89]	2009–10	WHO/ISH 2003	57	34.8	38	33.3
WEST						
Benin, Mixed [90]	2008	≥140/90 mmHg	42.7	27.9	-	-
Burkina Faso, Urban [91]	2004	≥140/90 mmHg	54.5	40.2	-	-
Gambia, Mixed [92]	1998–99	≥140/90 mmHg	43.7	18.4	-	-
Ghana, Rural [93]	2004–05	≥140/90 mmHg	42.4	25.4	24.1	25.9
Ghana, Mixed [94]	2004	≥140/90 mmHg	35.9	29.4	31.04	28.07
Ghana, Rural [95]	2003	≥140/90 mmHg	53	32.8	-	-
Ghana, Mixed [96]	2001	≥140/90 mmHg	54.7	28.7	29.9	28
Ghana, Rural [97]	2006–07	≥140/90 mmHg	53.5	35	37.2	34.1
Ghana, Rural [98]	2002–10	JNC 7. WHO/ISH 2003	66	24.1	25.7	22.5
Ghana, Rural [99]	2012	≥140/90 mmHg	53.84	44.7	-	-
Guinea, Mixed [100]	2003	≥140/90 mmHg	62	31.4	-	-
Guinea, Rural [101]	2001	≥140/90 mmHg	45.5	45.2	-	-
Liberia, Rural [102]	1991–92	≥140/90 mmHg	54.5	12.5	-	-
Nigeria, Mixed [103]	2010–11	JNC 6	71.1	34.7	-	-
Nigeria, Semi-urban [104]	2007–08	JNC 7	44.2	36.57	36.79	36.39
Nigeria, Semi-urban [105]	2011–12	JNC 7, WHO/ISH 2003	41.5	25.2	24.7	24.7
Nigeria, Rural [106]	2010–11	≥140/90 mmHg	57.3	44.5	49.3	42.3
Nigeria, Rural [107]	2012–13	JNC 7	41.3	20.2	20.5	20.1
Nigeria, Urban [108]	2006–10	JNC 7	41.9	33	38.3	27.8
Nigeria, Mixed [109]	2008	JNC 7	48.7	50.5	52	49.3
Nigeria, Rural [110]	2011	JNC 7	49.7	13.2	15	11.9
Nigeria, Urban [111]	1987–88	≥140/90 mmHg	36.35	31.1	34	17
Nigeria, Mixed [44]	1995	≥140/90 mmHg	49.5	14.5	14.7	14.3
Nigeria, Rural [112]	2005–06	WHO/ISH 2003	59.8	46.4	50.2	44.8
Nigeria, Semi-urban [113]	2012	≥140/90 mmHg	31.7	47	30.1	16.8
Nigeria, Mixed [114]	2009	≥140/90 mmHg	34.9	21.1	-	-
Nigeria, Semi-urban [115]	2002–03	JNC 6, WHO/ISH 1999	55	21	23.3	16.4
Nigeria, Rural [57]	2009–11	WHO/ISH 2003	45.3	21	-	-
Nigeria, Mixed [116]	2009–10	JNC 7	38.9	24.8	25.9	23.6
Nigeria, Semi-urban [117]	2011–12	≥140/90 mmHg	50	32.5	-	-
Nigeria, Urban [118]	2009–10	≥140/90 mmHg	43.88	34.8	-	-
Nigeria, Mixed [119]	2011–12	≥140/90 mmHg	41.7	31.8	33.5	30.5
Nigeria, Urban [120]	2006–07	≥140/90 mmHg	50.5	27.1	28.4	22.9
Nigeria, Rural [121]	2002–05	JNC 7	42.1	20.8	21.1	20.5
Nigeria, Urban) [122]	2007–08	≥140/90 mmHg	41.6	33	28.1	36.4

Table 4. Cont.

Country, Setting	Study period	Diagnostic criteria	Mean age (years)	Prevalence % (all)	Prevalence % (men)	Prevalence % (women)
Nigeria, Rural [123]	2004–05	≥140/90 mmHg	30.7	20.2	24.8	13.2
Nigeria, Semi-urban [124]	2011	JNC 7	50.5	15	18.8	12.5
Nigeria, Mixed [125]	2007–08	≥140/90 mmHg	40.8	32.8	-	-
Nigeria, Mixed [126]	2009–10	WHO/ISH 2003	38.02	42.2	46.3	37.7
Senegal, Urban [127]	1989–90	≥140/90 mmHg	31.45	22.5	23.6	21.5
Senegal, Urban [26]	2009	≥140/90 mmHg	69.5	65.4	63.9	67.1
Togo, Urban [128]	2009–10	≥140/90 mmHg	39	26.6	25.7	27.6
Togo, Urban [129]	2011	≥140/90 mmHg	40.8	36.7	34.6	38.4

JNC: Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure, WHO/ISH: World Health Organization/International Society of Hypertension.

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diastolic blood pressures were 129.6 mm Hg and 78.0 mm Hg respectively. Studies were mostly conducted on people aged ≥20 years, with an estimated overall mean age of 47.4 years, ranging from 30.7 to 76 years. For the age determination of subjects across selected studies, birth certificates were mostly employed, and in the absence of valid age-verification documents, subjects' age were determined from historical landmarks.

Prevalence and awareness rates of hypertension in Africa

Across all study settings, an elderly South African setting recorded the highest prevalence of hypertension in 2008 (77.3%, mean age 65 years) [23]. Other settings reporting higher prevalence rates of hypertension were also in older adult population surveys in Tanzania in 2010 (69.9%, mean age 76 years), Tunisia in 2003 (69.3%, mean age 69 years), and Senegal in 2009 (65.4%, mean age 69.5 years) respectively [24–26]. The lowest prevalence rates of hypertension were recorded in Sudan (7.5%, mean age 35 years) and Ethiopia (9.9%, mean age 36.1 years) in 1989 and 2008 respectively [27,28] (See **Table 4** for overall study characteristics).

The pooled crude prevalence in Northern Africa was higher than in sub-Saharan Africa (SSA), with hypertension prevalence of 33.3% in Northern Africa and 27.8% in sub-Saharan Africa. In other parts of SSA, Southern Africa recorded the highest prevalence, with a prevalence of 34.6% (males 35.4%, females 34.2%). Western Africa had a prevalence of 27.3% (males 29.6, females 28.2), Central Africa recorded 21.1% (males 21.5%, females 19.3%), and Eastern Africa had 26.8% (males 25.0, females 26.1) (see **Table 5** for details). The overall pooled crude prevalence (weighted means) of hypertension for Africa was 19.7% (males 23.0%, females 20.2%) in 1990, 27.4% (males 26.9, females 28.4) in 2000, and 30.8% (males 29.7, females 31.4). There were not huge differences in hypertension prevalence between urban and rural dwellers, with the exception of 1990, where urban dwellers recorded a prevalence of 17.2% (males 21.1, females 15.1), compared to 11.1% (males 9.4%, females 8.3%) recorded among rural dwellers (with urban and rural dwellers having prevalence of 26.1% versus 26.3% in 2000 and 29.6% versus 29.0% in 2010 respectively) (see **Table 6** for details).

Across selected studies, there is evidence suggesting the awareness of hypertension among people living with the disease has been increasing since 1990; however, the overall awareness rate still remains relatively low in many parts of Africa. From the pooled analysis, a weighted awareness rate (expressed as a percentage of cases of hypertension) of 16.9% was estimated in 1990, 29.2% in 2000 and 33.7% in 2010 (see **Tables 5 and 6** for details).

Modelled estimates of hypertension prevalence and number of cases in Africa

The modelling indicated the overall cases and prevalence of hypertension in Africa have been increasing since 1990. In adults aged ≥20 years, 54.6 million cases of hypertension were estimated in 1990 with an age-adjusted prevalence of 19.1% (13.9, 25.5), 92.3 million cases in 2000 with an age-adjusted prevalence of 24.3% (23.3, 31.6), 130.2 million cases in 2010 with an age-adjusted prevalence of 25.9% (23.5, 34.0), and a projected increase to 216.8 million cases of hypertension by 2030 with an age-adjusted prevalence of 25.3% (24.3, 39.7). The general sex distribution revealed the prevalence and number of cases of hypertension were higher among men than women. Among men, the prevalence and number of hypertension cases were both projected to increase between 2010 and 2030. About 29.8 million cases of hypertension were estimated in 1990 (21.2%, 95%CI: 16.5–29.6), 46.8 million cases in 2000 (25.1%, 95%CI: 22.9–31.0), 64.8 million cases in 2010 (26.1%, 95%CI: 23.6–33.6), and a projected increase to 112.1 million cases of hypertension by 2030 (26.4%: 24.5–41.1). However, there was a drop in prevalence among women between 2010 and 2030. 24.8 million cases of hypertension were estimated in 1990 (17.1%, 95%CI: 13.4–27.0), 45.5 million cases in 2000 (23.6%, 95%CI: 21.5–33.3), 65.4 million cases in 2010 (25.7%, 95%CI: 21.7–35.4), and a projected increase to 104.7 million cases of hypertension by 2030, with a drop in prevalence to 24.3% (95%CI: 22.4–38.9) (see **Tables 7–9** and **Figures 2–5**).

Discussion

This review provides an improved continent-wide estimate of the prevalence and awareness rates of hypertension in Africa using epidemiological modelling adjusted for age and sample size of the population. Having included studies conducted across various parts of Africa, the estimates may provide a close representation of the prevalence and the number of cases of hypertension in the continent.

From all studies, we estimated weighted mean systolic and diastolic blood pressures of 129.6 mm Hg and 78.0 mm Hg, respectively, with an overall mean age of 47.4 years. Our estimate is comparable with the estimates reported by Danaei and colleagues on the global trends of systolic blood pressure, with

Table 5. Regional pooled hypertension prevalence rates and mean blood pressures in Africa.

Main study characteristics			Prevalence and awareness of hypertension (%)				Weighted mean blood pressure (mm Hg)	
Region	Sample size	Mean age	Both sexes (se)	Male (se)	Female (se)	Awareness rate (se)	Mean systolic BP (se)	Mean diastolic BP (se)
North	28046	543	33.3 (2.6)	29.6 (2.1)	35.5 (2.6)	36.2 (9.2)	129.6 (1.6)	78.0 (0.8)
SSA	169688	464	27.8 (1.4)	27.8 (1.6)	27.8 (1.7)	30.6 (3.1)	125.6 (0.9)	78.9 (0.5)
Central	24206	437	21.1 (2.7)	21.5 (3.1)	19.3 (2.9)	25.1 (4.2)	119.2 (1.8)	75.4 (0.9)
East	53312	460	26.8 (2.9)	25.0 (2.8)	26.1 (3.4)	40.9 (6.9)	127.5 (2.2)	79.3 (0.8)
South	34753	475	34.6 (4.2)	35.4 (5.1)	34.2 (4.6)	26.4 (7.0)	123.5 (2.3)	79.4 (0.9)
West	57417	469	27.3 (1.5)	29.6 (1.8)	28.2 (1.9)	21.7 (2.7)	128.2 (0.9)	79.8 (0.8)

SSA: sub-Saharan Africa, se: standard error.
doi:10.1371/journal.pone.0104300.t005

Table 6. Pooled crude prevalence and awareness of hypertension from all studies.

Main study characteristics			Prevalence and awareness of hypertension (%)				Weighted mean blood pressure (mm Hg)	
Setting	Sample size	Mean age	Both sexes (se)	Male (se)	Female (se)	Awareness rate (se)	Systolic (se)	Diastolic (se)
1990								
Mixed	21416	441	19.7 (2.9)	23.0 (3.3)	20.2 (3.5)	16.9 (3.9)	123.8 (22)	77.5 (1.1)
Urban	6925	394	17.2 (3.5)	21.1 (4.0)	15.1 (3.5)	-	-	-
Rural	5796	488	11.1 (2.1)	9.4 (3.0)	8.3 (4.4)	-	-	-
2000								
Mixed	38294	512	27.4 (2.1)	26.9 (2.1)	28.4 (2.5)	29.2 (4.5)	126.9 (1.8)	77.2 (0.9)
Urban	20898	457	26.1 (1.9)	26.8 (1.5)	23.9 (1.9)	-	-	-
Rural	11377	552	26.3 (2.3)	24.5 (3.2)	25.7 (3.1)	-	-	-
2010								
Mixed	126754	471	30.8 (1.6)	29.7 (1.9)	31.4 (2.1)	33.7 (3.9)	126.9 (1.1)	79.4 (0.5)
Urban	44114	474	29.6 (2.1)	28.2 (2.3)	28.4 (2.5)	-	-	-
Rural	46669	486	29.0 (2.3)	26.9 (2.7)	30.1 (2.9)	-	-	-

se: standard error.
doi:10.1371/journal.pone.0104300.t006

Table 7. Estimated hypertension prevalence rates and cases in Africa in both sexes (estimates derived from epidemiological model and UN population demographics).

Age (years)	1990		2000		2010		2030	
	Prevalence (%) = $8.7962e^{0.0161x}$	Hypertension cases (000)	Prevalence (%) = $11.822e^{0.0177x}$	Hypertension cases (000)	Prevalence (%) = $9.7956^{0.0233x}$	Hypertension cases (000)	Prevalence (%) = $10.081e^{0.0213x}$	Hypertension cases (000)
20–24	12.5	6961.279	17.5	13134.411	16.4	15969.503	16.2	24372.870
25–29	13.6	6319.733	19.1	11761.160	18.5	15499.070	18.0	23390.362
30–34	14.7	5722.049	20.8	10540.253	20.8	14395.931	20.1	22549.551
35–39	15.9	5125.030	22.8	9662.284	23.4	12993.072	22.3	21855.722
40–44	17.3	5293.178	24.9	8844.815	26.3	11868.440	24.9	21339.520
45–49	18.7	4770.732	27.2	7956.942	29.6	11178.983	27.7	20226.663
50–54	20.3	4416.345	29.7	7076.878	33.2	10531.041	30.8	18005.650
55–59	22.0	4015.862	32.4	6135.655	37.4	9602.545	34.3	15692.831
60–64	23.9	3546.226	35.4	5372.853	42.1	8458.233	38.2	13671.611
65–69	25.9	2935.649	38.7	4436.133	47.3	6989.765	42.6	11683.620
70–74	28.0	2333.696	42.3	3326.293	53.2	5546.874	47.4	9193.002
75–80	30.4	1713.440	46.2	2078.889	59.8	3809.200	52.9	7714.551
80+	35.7	1462.513	55.1	1997.851	75.7	3327.737	65.4	7132.029
Total 20+ (95% CI)	19.1 (13.9–25.5)	54615.730	24.3 (23.3–31.6)	92324.390	25.9 (23.5–34.0)	130170.401	25.3 (24.2–39.7)	216828.010

x = mid-point of UN population 5-year age group.

doi:10.1371/journal.pone.0104300.t007

Table 8. Estimated hypertension prevalence rates and cases in Africa among men (estimates derived from epidemiological model and UN population demographics).

Age (years)	1990		2000		2010		2030	
	Prevalence (%) = $10.505e^{0.0175x}$	Hypertension cases (000)	Prevalence (%) = $17.771e^{0.0098x}$	Hypertension cases (000)	Prevalence (%) = $10.334e^{0.0223x}$	Hypertension cases (000)	Prevalence (%) = $11.966e^{0.0193x}$	Hypertension cases (000)
20–24	15.4	4287.483	21.6	8141.867	16.9	8241.670	17.9	13606.260
25–29	16.9	3901.526	22.5	6946.029	18.9	7934.829	19.6	12816.871
30–34	18.4	3542.458	23.6	5932.465	21.1	7345.081	21.5	16039.680
35–39	20.1	3187.968	24.6	5185.153	23.6	6596.039	23.6	11574.670
40–44	21.9	2865.689	25.7	4513.438	26.4	5943.763	25.8	11090.801
45–49	23.9	2535.072	26.8	3859.029	29.5	5490.843	28.3	10275.230
50–54	26.1	2303.794	28.1	3261.431	32.9	5063.796	30.9	8962.983
55–59	28.5	2061.997	29.3	2667.812	36.8	4529.248	34.0	7618.278
60–64	31.1	1755.050	30.7	2197.312	41.2	3918.656	37.2	6406.076
65–69	33.9	1365.244	32.0	1718.733	46.0	3154.577	40.8	5243.806
70–74	37.0	978.408	33.5	1201.287	51.5	2424.530	44.7	3917.635
75–80	40.4	589.023	34.9	695.730	57.5	2238.964	48.9	2538.670
80+	48.2	411.868	38.2	464.571	71.9	1917.733	58.8	2022.895
Total 20+ (95% CI)	21.2 (16.5–29.6)	29785.580	25.1 (22.9–31.0)	46784.860	26.1 (23.6–33.6)	64799.730	26.4 (24.5–41.1)	112114.210

x = midpoint of UN population 5-year age group.

doi:10.1371/journal.pone.0104300.t008

Table 9. Estimated hypertension prevalence rates and cases in Africa among women (estimates derived from epidemiological model and UN population demographics).

Age (years)	1990		2000		2010		2030	
	Prevalence (%) = $7.631e^{0.0193x}$	Hypertension cases (000)	Prevalence (%) = $14.879e^{0.0155x}$	Hypertension cases (000)	Prevalence (%) = $7.6974e^{0.0279x}$	Hypertension cases (000)	Prevalence (%) = $8.7533e^{0.0227x}$	Hypertension cases (000)
20–24	11.7	3253.603	19.2	7188.909	14.2	6879.980	14.7	11003.651
25–29	12.9	3018.326	20.3	6265.350	16.3	6839.885	16.6	10705.340
30–34	14.2	2791.264	21.5	5463.243	18.8	6477.360	18.7	10444.901
35–39	15.7	2548.505	22.8	4870.534	21.6	5970.342	21.0	10247.020
40–44	17.3	2320.801	24.1	4347.172	24.8	5617.575	23.7	10144.220
45–49	19.1	2108.716	25.5	3814.806	28.7	5480.796	26.7	9787.847
50–54	21.1	1978.743	27.1	3309.921	32.8	5355.558	30.0	8847.015
55–59	23.2	1800.967	28.7	2818.021	37.8	5053.976	33.8	7864.990
60–64	25.6	1593.129	30.4	2429.126	43.4	4600.255	38.0	7056.223
65–69	28.2	1289.237	32.2	1960.988	49.9	3955.928	42.8	6247.986
70–74	31.1	976.8551	34.1	1457.391	57.4	3280.345	48.2	5124.622
75–80	34.3	630.250	36.1	906.116	65.9	2970.846	54.3	3631.026
80+	41.6	519.756	40.5	707.961	87.2	2887.797	68.8	3609.290
Total 20+ years (95% CI)	17.1 (13.4–27.0)	24830.150	23.6 (21.5–33.3)	45539.541	25.7 (21.7–35.4)	65370.642	24.3 (22.4–38.9)	104714.131

x = midpoint of UN population 5-year age group.

doi:10.1371/journal.pone.0104300.t009

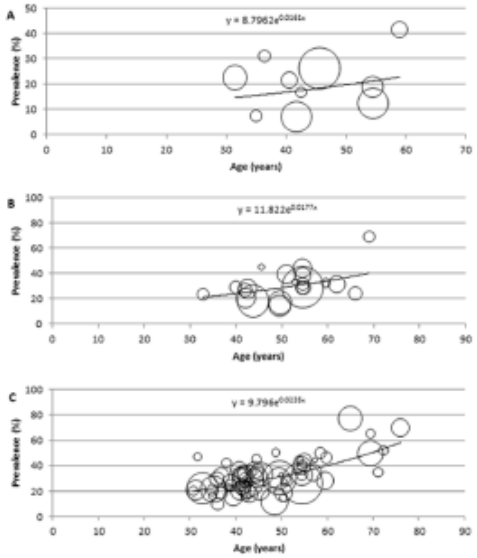

Figure 2. Epidemiological model showing distribution of hypertension prevalence according to age in both sexes, with size of bubble corresponding to respective sample size (A: 1990, B: 2000, C: 2010).
doi:10.1371/journal.pone.0104300.g002

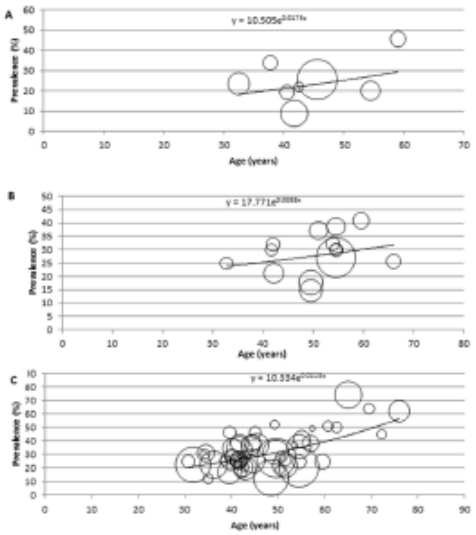

Figure 3. Epidemiological model showing distribution of hypertension prevalence according to age among men, with size of bubble corresponding to respective sample size (A: 1990, B: 2000, C: 2010).
doi:10.1371/journal.pone.0104300.g003

an overall mean SBP in SSA ranging 129.2–132.7 mm Hg and 132.6–134.8 mm Hg among men and women, respectively, between 1981 and 2008 [29]. This study further supports our finding of a high prevalence of hypertension in Africa, with the highest value of SBP globally estimated in SSA (along with central and eastern Europe) [29].

Across selected studies, higher prevalence rates of hypertension were reported with increasing age of subjects. This is underpinned by previous research findings where increasing age is associated with significant increase in the prevalence of hypertension, especially in people aged ≥60 years [12,21]. For example, a higher prevalence of hypertension was reported in Northern Africa with a pooled prevalence of 33.3% compared to a prevalence of 27.8% in SSA. This could be partly explained by age difference, with a mean age of 54.3 years in Northern Africa, compared to 46.4 years in SSA. In the 2009 hospital-based Epidemiological Trial of Hypertension in North Africa (ETHNA), a high prevalence (45.4%, mean age 49.2 years) was also reported for Northern Africa [30]; this further supports findings of this study.

A higher prevalence of hypertension was noted among urban dwellers from the pooled estimates mainly in 1990 (urban 17.2%, rural 11.1%), while the prevalence was virtually the same in years 2000 and 2010. The narrowing of prevalence gaps between urban and rural dwellers in years 2000 and 2010 could be due to a possible reverse rural-urban migration, which has been reported when urban dwellers fail to cope with the economic challenges and vulnerabilities associated with urban life, and may prefer to return to natural resource-rich rural settlements [31]. In addition, there are reports that even in rural settings, the apparent remote and traditional styles do not seem to protect them again, as more of these rural settings are gradually becoming semi-urbanized [3].

Opie and colleagues also argued that many site-specific hypertension prevalence estimates in Africa may not truly reflect the burden in these settings, as there are still doubts on the proportion of Africans that truly reside in rural settings [32].

Meanwhile, an increasing, yet low, awareness rate of hypertension in Africa was reported, with pooled weighted awareness rate of 16.9% in 1990, 29.2% in 2000 and 33.7% in 2010. This estimate, to the best knowledge of our knowledge, remains the first weighted continent-wide awareness rate of hypertension reported in Africa, and thus forms an important finding of this study. The low awareness rate reported may still reflect a poor response to management of hypertension in the continent [33]. Kayima et al. corroborates this, reporting a very low awareness rate of hypertension ranging between 8% and 10% in Africa in the early 2000s [8].

In this review, the general sex distribution showed that the prevalence and cases of hypertension were higher among men than women. This is also in line with many reports in Africa [3,8].This may be because the overall mean age from all selected studies was 47.4 years, which is just about a reported mean menopause age of 49.4 years among African women [34], and there is established evidence of a steeper blood pressure rise in men than women before the age of menopause [35]. We further estimated that there was a drop in hypertension prevalence among women between 2010 and 2030; Danaei and colleagues reported similar findings between 1981 and 2008, where, in contrast to a predominant rise in mean SBP among men, the mean SBP among women increased only in two countries globally between 1981 and 2008 [29]. Our estimate may therefore just be reflective of a continuation in this trend. Still, from the modelling, over 54.6 million cases of hypertension were estimated in 1990 (19.1%), 92.3

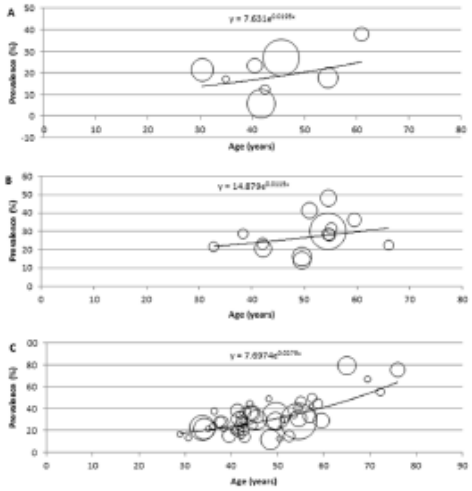

Figure 4. Epidemiological model showing distribution of hypertension prevalence according to age among women, with size of bubble corresponding to respective sample size (A: 1990, B: 2000, C: 2010).
doi:10.1371/journal.pone.0104300.g004

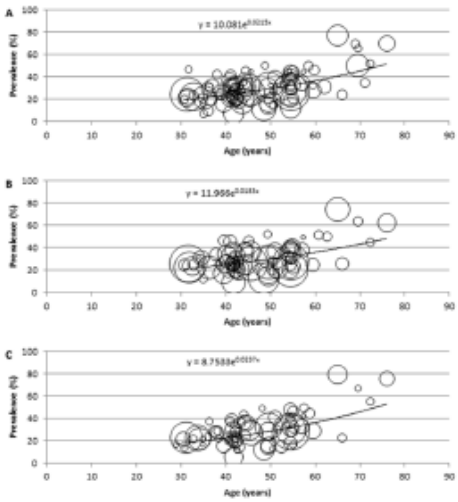

Figure 5. Epidemiological model showing distribution of hypertension prevalence according to age (projections for 2030), with size of bubble corresponding to respective sample size (A: both sexes, B: men, C: women).
doi:10.1371/journal.pone.0104300.g005

million cases in 2000 (24.3%), 130.2 million cases in 2010 (25.9%), and a projected increase to 216.8 million cases of hypertension by 2030 (25.3%). These estimates are higher than the 20 million reported by WHO African regional office (AFRO) in 2005 [36]. The WHO AFRO estimate was based on ≥160/95 mm Hg and this is probably the reason for the low hypertension cases reported. However, reports show that this figure has often been quoted in many official documents as the number of hypertension cases in Africa [4]. Meanwhile, Twagirumukiza et al. estimated about 75 million cases (16.2%) of hypertension among people aged ≥15 years in SSA in 2008, and projected to increase to 125.5 million cases (17.4%) in 2025 (**Table 10**) [15]. These figures are relatively low compared to the current estimates. It is understandable that these estimates were for SSA and that the mean age was low (40 years), they may yet not reflect the true burden of hypertension in the continent, as their review and analysis mainly included studies from 11 countries in Africa. In addition, another reviewer also noted these concerns, and agreed the estimates were very low compared to recent prevalence rates reported in Africa, and may be erroneously interpreted that the burden of hypertension in the continent is low [37]. However, Kearney et al. reported higher hypertension estimates, with about 79.8 million hypertension cases (27.6%) estimated among people aged ≥20 years in 2000 and projected to reach about 150.7 million cases (27.7%) in 2025 [6]. These prevalence rates are comparable with the current estimates, but the difference in the number of hypertension cases may be due to the fact that demographic changes as reported by the United Nations population projections were considered. Kearney et al. also reported a minimal change in hypertension prevalence rates between 2000 and 2025 (27.6% versus 27.7%) [6], which is also comparable with the current estimates for 2000 and 2030 (24.3% versus 25.3%) (**Table 10**). This may be due to a potentially better public health response to the overall management of hypertension in many African countries.

Study limitations

The study aims to provide an improved continent-wide estimate of hypertension in Africa using current definitions (cut off "≥140/90 mm Hg"). However, the study has some important limitations. First, the modelling was age-dependent, we understand there are other important social and health determinants that could have resulted in varying estimates if considered, including, but not limited to the overall population characteristics, socio-economic factors and general living conditions [38]. In addition, the overall mean age was 47.4 years, which could also have resulted in a lower prevalence estimate, as research evidences show significant increase in hypertension prevalence in people aged ≥60 years [21]. Second, all studies included in our modelling were based on the blood pressure cut off "≥140/90 mm Hg"; notwithstanding, some studies have varying designs and blood pressure measuring protocols, which could have affected the quality of the current estimates. Moreover, while we ensured all studies that were graded as *high* and *moderate quality* were included in the quantitative analysis, some *low quality* studies were also included in the quantitative analysis on the basis of good study designs, which could potentially affect our overall estimates (See **Box S1**, **Table S1** and **Table S2** in **File S1**).

Third, not all studies reported age- and sex- specific estimates, including urban or rural site-specific estimates, as an epidemiology of the prevalence of hypertension in these sub-groups could have been further helpful. Furthermore, the incompleteness of data across many studies prevented us from providing estimates on the control and treatment of hypertension in Africa. We still hope that providing a continent-wide estimate of the awareness rate of hypertension may further give a general view of the public health response to the disease in the continent. However, we extracted data from 92 studies conducted in 31 African countries (having overall sample size of 197734), and with a consideration of the United Nations population demographics in the epidemiological

Table 10. Comparable estimates of hypertension prevalence rates from selected studies.

	Current Study*			Kearney et al.* [6]		Twagirumukiza et al.** [15]	
	2000	2010	2030	2000	2025	2008	2025
Prevalence rate (%)	24.3	25.9	25.3	27.6	27.7	16.2	17.4

*20years (all Africa).
**15-years (sub-Saharan Africa).
doi:10.1371/journal.pone.0104300.t010

modelling. The current estimates may therefore provide fair representation of the overall African population and better reflect the prevalence and number of cases of hypertension in the continent.

Challenges and public health response to hypertension in Africa

Recent reports show that the World Heart Federation, supported by the Pan African Society of Cardiology (PASCAR), has been actively building capacities across Africa to address the rising burden of hypertension and other cardiovascular diseases in the continent [39]. However, collaborations and response within Africa remains poor, as hypertension still ranks low among health priorities, owing to competition for the limited resources from a co-existing high burden of infectious diseases [5]. Moreover, in countries with some levels of care for hypertension, the standards of health service delivery is poor [3]. Many cases of hypertension are detected late, treatments rarely follow standard guidelines, and the costs of medications are generally high [35]. Besides, health care seeking behaviour has also been affected, with people often preferring low-cost substandard health facilities [40]. This is particularly a problem in rural settings where the prevalence of hypertension has been reported to be on a gradual increase [8]. Further reports show that even with a relatively lower prevalence of hypertension among rural dwellers, the detection and overall management are poor in comparison to urban dwellers [3]. Additionally, many African countries are yet to implement population-wide control measures to address risk factors for hypertension [41], even with confirmed reports of high salts and fats consumption in the region and evidence showing cost-effectiveness of interventions targeting this [42,43]. The WHO now recommends country-specific initiatives and legislation concerning food labelling and products formulation, including sodium and saturated fats content in processed foods [2,39].

Conclusions

This study suggests a high prevalence of hypertension in Africa, and the awareness of the disease, though increasing, still remains low. Hypertension deserves to be on the health priority lists of African nations, and problems with funding may possibly be reduced by partnering with leading international bodies for cardiovascular diseases. Essentially, policy makers and stakeholders in the health sector need to institute nationwide population-based strategies towards creating awareness on hypertension and educating people on the main risk factors such as smoking, harmful use of alcohol, sedentary lifestyles and unhealthy diets. It is hoped that the findings of this review may prompt appropriate policy response at country level towards improved detection, control and overall management of hypertension in Africa.

Supporting Information

Checklist S1 PRISMA Checklist.
(DOC)

File S1 Box S1, Brief details of quality criteria of retained studies on hypertension in Africa. (This is a description of how studies were graded and assessed). Table S1, Quality assessment and grading of retained hypertension studies in Africa. (This shows the grading of each study). Table S2. Overall study characteristics with site identification numbers. (This shows all retained study sites with identification numbers used for grading)
(DOCX)

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Author Contributions

Conceived and designed the experiments: DA. Performed the experiments: DA. Analyzed the data: DA CB. Contributed reagents/materials/analysis tools: DA CB. Wrote the paper: DA CB.

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An Estimate of the Incidence and Prevalence of Stroke in Africa: A Systematic Review and Meta-Analysis

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Abstract

Background: Stroke is increasingly becoming a challenging public health issue in Africa, and the non-availability of data has limited research output and consequently the response to this burden. This study aimed to estimate the incidence and prevalence of stroke in Africa in 2009 towards improved policy response and management of the disease in the region.

Methods: A systematic search of Medline, EMBASE and Global Health for original population-based or hospital-based studies on stroke was conducted. A random effect meta-analysis was conducted on crude stroke incidence and prevalence rates, and a meta-regression-like epidemiological model was applied on all data points. The fitted curve generated from the model was used to estimate incident cases of stroke and number of stroke survivors in Africa at midpoints of the United Nation population 5-year age groups for the year 2009.

Results: The literature search yielded a total of 1227 studies. 19 studies from 10 African countries were selected. 483 thousand new stroke cases among people aged 15 years or more were estimated in Africa in 2009, equivalent to 81.2 (13.2–94.9)/100,000 person years. A total of 1.89 million stroke survivors among people aged 15 years or more were estimated in Africa in 2009, with a prevalence of 317.3 (314.0–748.2)/100000 population. Comparable figures for the year 2013 based on the same rates would amount to 535 thousand (87.0–625.3) new stroke cases and 2.09 million (2.06–4.93) stroke survivors, suggesting an increase of 10.8% and 9.6% of incident stroke cases and stroke survivors respectively, attributable to population growth and ageing between 2009 and 2013.

Conclusion: The findings of this review suggest the burden of stroke in Africa is high and still increasing. There is need for more research on stroke and other vascular risk factors towards instituting appropriate policy, and effective preventive and management measures.

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Introduction

The burden of stroke is increasing in many low- and middle-income countries (LMIC) [1], and due to high fatality rates and overwhelming resource incurred by the health systems, stroke and many non-communicable diseases (NCDs) are now targeted public health priorities in these regions [2,3]. Globally, about 16 million new cases of stroke and 62 million stroke survivors were estimated in 2005, with deaths from stroke accounting for 9.7% of all global deaths, and this is expected to increase to over 23 million new stroke cases and 7.8 million stroke deaths by 2030 in the absence of significant global public health response [4,5].

It has been estimated that LMIC account for over 87% disability adjusted life years (DALYs) from stroke, which is about seven times the DALYs lost in high-income countries (HIC) [6]. Africa is particularly worst hit, owing to population growth, unchecked industrialization and increased consumption of western diets, leading to a rise in many modifiable vascular disease risk factors including smoking, harmful use of alcohol, physical inactivity and unhealthy diets, and invariably resulting in increased prevalence of hypertension, diabetes and obesity [7,8]. In 2000, two African countries, although recorded low stroke prevalences, had remarkably high stroke incidence rates [9]. According to GBD 2002 estimates, three African countries (Angola, Liberia and Sierra Leone) recorded the highest stroke mortalities and DALYs worldwide [5,10]. Between 2002 and 2004, estimates further revealed an increasing prevalence with 8% of new stroke cases and 5% of stroke survivors occurring in Africa [5,11]. Even with this increasing burden, the public health response, accesses to health services and treatment options in many African countries have been poor [7,12]. Specifically, the lack of functional stroke units, neurologists, health workers, cranial computed tomography (CT) scans, magnetic resonance imaging (MRI) machines and echo-doppler machines, among many others, has negatively affected stroke outcomes [2,12]. Moreover, the high cost of medical care in a relatively low-income African society could have resulted in high stroke fatalities, as some studies have

indicated that stroke prevalence and deaths in Africa increased due to an overtly poor socioeconomic status [6]. For example, a recent study revealed the incidence of stroke in HIC decreased by over 40% between 1970 and 2008, but with actual number of stroke cases increasing due to ageing of the population [13], while in Africa and many LMIC, stroke incidence rose by over 100% over the same period [13]. Furthermore, due to the high proportion of undiagnosed hypertension in Africa especially among the younger population [14], stroke incidence has also been reported to be more severe and higher among the active and productive population age groups [15].

Meanwhile, the World Health Organization (WHO) technically supported her member countries with methods for improved data collation and registration of hospital stroke cases [16]. Notwithstanding, another set-back in the response to the management of stroke in Africa is the lack of data and low research output [7,14]. Stroke case ascertainment and survey methodologies have not, in most cases, complied with international protocols [7]. Published research studies are characterized by poorly organized community-based studies, difficulties in making retrospective diagnosis, and overlapping cases of first and recurrent strokes [7,17]. The few studies on stroke, therefore, could have been marked by underestimation of the stroke burden in Africa. In view of this high burden of stroke, its public health importance, and the relatively low research output in Africa, this study aimed to estimate the incidence and prevalence rates of stroke in Africa in order to attempt to quantify the burden and inform decision regarding policy responses and health system interventions across many countries in the region.

Methods

Search strategy and selection criteria

After identification of relevant Medical Subject Headings (MESH) and keywords, a final search strategy was developed. Searches were conducted in three main databases: Medline, EMBASE and Global Health. The search date was set from January 1970 to December 2013. An additional search was conducted on Google Scholar and reference lists of relevant studies to identify publications that could have been omitted in the database searches. The search terms employed on Medline are shown in **Table 1**, while those employed on other databases are shown in **Table S1** and **Table S2** in **File S1**.

Studies included for further screening were mainly population/community- and hospital-based studies on stroke in Africa, conducted on or after 1970 and providing numerical estimates on the incidence and/or prevalence of stroke in the region. African countries were as defined by the World Bank list of economies (October 2013) [18]. Studies conducted before 1970, without numerical estimates, on non-human subjects, and that were mainly reviews were excluded. Studies with well-defined stroke diagnostic criteria and survey protocols were further retained. Due to the paucity of data, varying sources of information including demographic health surveys, community-based door-to-door surveys, hospital records and outpatient clinics were allowed. However, the final stroke case ascertainment complied with the standard WHO definition, defined as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting longer than 24 hour, unless interrupted by death, with no apparent cause other than that of vascular origin" [19,20]. According to experts, new cases of stroke were defined as number of people presenting with first ever stroke in a given period, while

Table 1. Search terms (Medline).

#	Searches
1	africa/or africa, northern/or algeria/or egypt/or libya/or morocco/or africa, central/or cameroon/or central african republic/or chad/or congo/or "democratic republic of the congo"/or equatorial guinea/or gabon/or africa, eastern/or burundi/or djibouti/or eritrea/or ethiopia/or kenya/or rwanda/or somalia/or sudan/or tanzania/or uganda/or africa, southern/or angola/or botswana/or lesotho/or malawi/or mozambique/or namibia/or south africa/or swaziland/or zambia/or zimbabwe/or africa, western/or benin/or burkina faso/or cape verde/or cote d'ivoire/or gambia/or ghana/or guinea/or guinea-bissau/or liberia/or mali/or mauritania/or niger/or nigeria/or senegal/or sierra leone/or togo/
2	exp vital statistics/or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	stroke/or brain infarction/or brain stem infarctions/or cerebral infarction/or stroke, lacunar/
13	cerebrovascular accident.mp.
14	cerebrovascular disease.mp.
15	CVA.mp.
16	12 or 13 or 14 or 15
17	1 and 11 and 16

doi:10.1371/journal.pone.0100724.t001

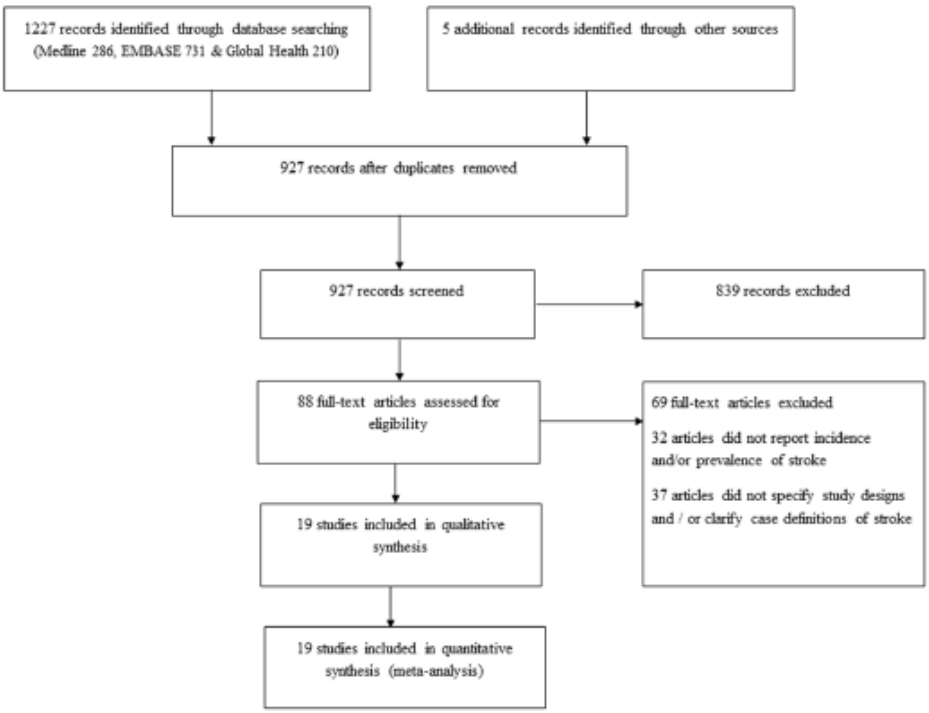

Figure 1. Flow diagram of search strategy.
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stroke survivors were the total number of people who have had stroke or living with its sequelae at a given time [20,21]

Data extraction and statistical analysis

An independent parallel search and double extraction was conducted and all extracted data was stored in a Microsoft Excel file format. Data were abstracted systematically on study location, study period, mean age or age range, person years or sample size, incident cases of stroke or number of stroke survivors, and their respective age- and sex-specific incidence or prevalence rates. These were sorted into population-based or hospital-based data separately for analysis. For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were compared for consistency and included in the selected paper.

From reported overall crude incidence or prevalence of stroke in a given cohort, a random effect meta-analysis was conducted with pooled effect of stroke expressed per 100,000 person years or population respectively. The overall data estimates of age- and sex-specific prevalence and incidence from all studies were used in our modelling (see **Table S3** in **File S1**). A meta-regression-like epidemiological model in the form of a bubble graph was applied (done separately for males and females), adjusted for mean ages and the crude prevalence and incidence rates of stroke from all studies, with the size of the bubble corresponding to the given sample size. The fitted curve explaining the largest proportion of variance (best fit) was applied. From all data points, the median year of study was estimated, and the equations generated from the modelled curves were then separately used to estimate the new cases of stroke and number of stroke survivors at midpoints of the United Nation (UN) population 5-year age groups for the estimated median year. Africa populations were determined from the 2012 United Nations population demographics [22]. All statistical analyses were conducted on Stata 13.1 (Copyright 1985-2013 StataCorp LP).

Results

Systematic review

The literature search returned 1227 publications from Medline (286), EMBASE (731) and Global Health (210). A further 5 studies were included from other sources (Google Scholar and reference lists of relevant publications). 927 studies remained after removing duplicates. On screening titles for relevance (stroke studies conducted primarily on African populations), 839 studies were excluded, giving a total of 88 full texts that were assessed. After applying the quality criteria, 69 studies were further excluded (32 articles did not provide numerical estimates on incidence and/or prevalence of stroke, and 37 articles did not clarify study designs and survey methodologies). A total of 19 studies were finally retained for the review (**Figure 1**).

Table 2. Overall characteristics of retained studies.

Country, Location, Setting	Author, Year	Study period	Survey method	Case definition
EASTERN AFRICA				
Ethiopia, Rural communities [23]	Tekle-Haimanot et al. 1990	1986–88	A door-to-door survey	WHO definition
Tanzania, Hai District, Rural [24]	Dewhurst et al. 2013	1 November 2009 and 31 July 2010	Point prevalence of stroke estimated from a cross-sectional two-phased community epidemiological survey.	WHO International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)
Tanzania, Hai district & Dares Salaam, Mixed Rural and Urban [25]	Walker et al. 2010	2003–06	Stroke incidence measured in two well defined demographic surveillance sites (DSS) over a 3-year period. Patients who had first-ever or recurrent strokes were included. Patients were excluded in suspected cases of infection or a space-occupying lesion	WHO definition
NORTHERN AFRICA				
Egypt, Al Kharga district, Mixed [26]	Farghaly et al. 2013	June 1, 2005 to May 31, 2009	A door-to-door screening including every door was carried out using a standardized questionnaire	WHO definition
Egypt, Al Quseir. Urban [27]	El Tallawy et al. 2013	July 1, 2009 to January 31, 2012	A door-to-door survey of every household in the district	WHO definition
Egypt, Assuit, Urban [28]	Khedr et al. 2013	January 1 2010 - December 31 2010	Community-based study using a three phase door-to-door survey	WHO definition
Egypt, Sohag, Mixed Urban and Rural [29]	Kandil et al. 2006	January 1st 1992 to April 30, 1993	Multistage, systematic random sampling using a door-to-door survey	WHO definition. Diagnosis confirmed by CT scan and other laboratory investigations creatinine
Libya, Benghazi, Urban [30]	El Zunni et al. 1995	January 1991 to December 1993	Survey conducted on patients referred from the walk-in polyclinics to the four university hospitals and to a rehabilitation center for the handicapped.	Cranial CT scan was performed on all cases within the first week of onset of stroke
Libya, Benghazi, Urban [31]	Ashok et al. 1986	November 1, 1983 and October 31, 1984	Hospital-based survey conducted on referred patients with neurological problems	Cranial CT was performed on cases within the first week of onset of stroke. Survey based on the US National Survey of Stroke guidelines
Tunisia, Kelibia, Mixed Urban and Rural [32]	Attia Romdhane et al. 1993	1985	Population-based survey	WHO definition and neurologic tool
SOUTHERN AFRICA				
Mozambique, Maputo, Urban [33]	Damasceno et al. 2010	August 1, 2005, to July 31, 2006	Hospital-based survey using the STEPS Stroke questionnaire. Both first-ever and recurrent stroke events were registered	WHO definition: "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin."
South Africa, Agincourt Health and Population Unit, Limpopo province, Rural [34]	Connor et al. 2004	August 2001-October 2002	Point prevalence of stroke survivors measured through door-to-door demographic health survey. Person's first-ever-in-a-lifetime event was recorded	WHO definition: "rapidly developing signs of focal (or global) disturbance of cerebral function, leading to death or lasting longer than 24 hours, with no apparent cause other than vascular". Person's first-ever-in-a-lifetime event was recorded
South Africa, Atteridgeville and Mamelodi suburban areas of Pretoria, Urban [35]	Rosman 1986	May 1 1984-April 30 1985	Prospective hospital-based survey. Included all strokes (first-ever and recurrent)	Diagnosis confirmed by cranial CT
Zimbabwe, Harare, Urban [36]	Matenga 1997	Jan- Dec 1991	A hospital-based stroke registry survey. Only first-ever strokes were included	Stroke was defined according to the WHO definition. None had CT
WESTERN AFRICA				
Benin, Cotonou, Urban [37]	Cossi et al. 2012	September 15, 2008-May 15, 2009	A three-phase door-to-door study was performed	Diagnosis of stroke was confirmed by CT scan evaluation
Nigeria, Ibadan, Urban [38]	Osuntokun et al. 1979	1973–75	Population-based stroke registry survey	WHO definition
Nigeria, Igbo-Ora, Rural [39]	Osuntokun et al. 1987	1982	Community-based door-to door survey	WHO definition

Table 2. Cont.

Country, Location, Setting	Author, Year	Study period	Survey method	Case definition
Nigeria, Lagos, Urban [40]	Danesi et al. 2013	January 1st and December 31st 2007	Prospective community-based stroke registry enrolling hospitalized and non-hospitalized first-ever in a lifetime stroke cases presenting at all health facilities	Stroke was defined using the WHO clinical criteria 'sudden onset of focal neurological deficit lasting longer than 24 h or leading to death with no other cause other than a vascular event'
Nigeria, Lagos, Urban [41]	Danesi et al. 2007	June 1, 2005, and May 30, 2006	Population-based, door-to-door survey using modified WHO questionnaire	Stroke defined as "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin."

CT: computed tomography, ICD: International Classification of Disease, WHO: World Health Organization
doi:10.1371/journal.pone.0100724.t002

Study characteristics

The retained 19 studies [23–41] were conducted across the main regions of Africa (east, north, west and south), but with Northern Africa having the highest output (7 studies). 10 African countries were represented; Egypt and Nigeria ranked highest with 4 studies each, Libya, South Africa and Tanzania had two studies each, while Benin, Ethiopia, Mozambique, Tunisia and Zimbabwe had one study each. Most studies (84.2%) were completed within one year period and the median year of study from all data points was 2009. About 57.9% of studies were conducted in predominantly urban settings. The total sample size from all retained studies was over 6.3 million, with a mean and median sample size of 332,276.5 and 60,820 respectively. 14 studies were population-based, of which 8 were community-based door-to-door surveys and 2 studies each were based on demographic health surveys, population/community-based stroke registries and cross-sectional population-based surveys. There were 5 hospital-based studies with only one from a hospital-based stroke registry. Studies comply with the WHO case ascertainment or a modified definition, while some studies employed cranial computed tomography (CT) or magnetic resonance imaging (MRI) to confirm diagnosis (**Table 2**). Most studies were conducted on

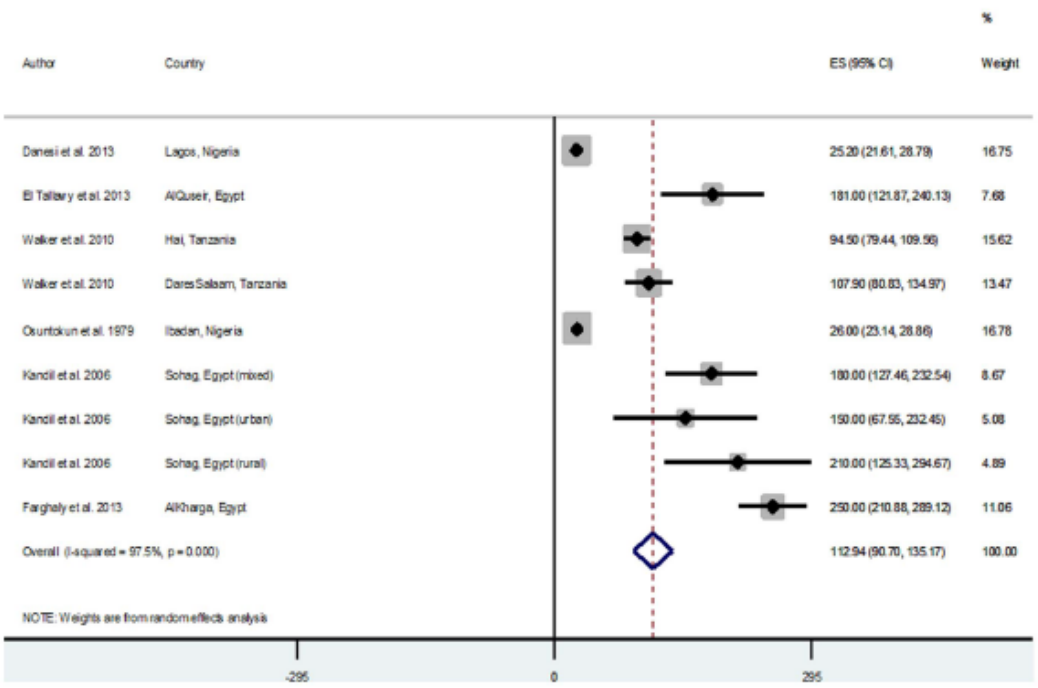

Figure 2. Pooled crude incidence rates of stroke from population-based studies.
doi:10.1371/journal.pone.0100724.g002

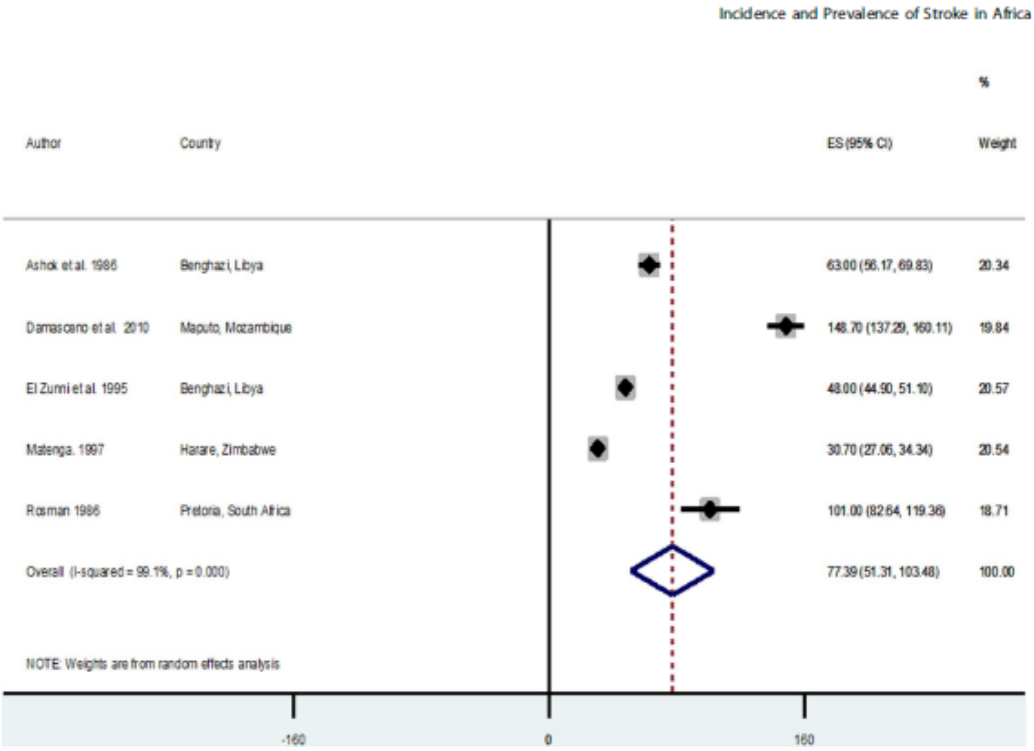

Figure 3. Pooled crude incidence rates of stroke from hospital-based studies.
doi:10.1371/journal.pone.0100724.g003

the entire study population with an overall mean age of 55.9 years. Across retained studies, age determination of subjects were determined from documented age-verification records, and in the absence of such, historical landmarks were employed.

Pooled estimates of reported crude stroke incidence and prevalence rates

Across studies reporting crude incidences of stroke, there were 6 population/community-based and 5 hospital-based studies. Population-based incidence rates were generally higher ranging from 25.2/100,000 person years (py) and 26.0/100,000 py in Lagos and Ibadan Nigeria in 2007 and 1979 respectively [38,40], to 250/100,000 py in Al-Kharga Egypt in 2007 [26]. The hospital-based studies reported lower incidence rates ranging from 30/100,000 py in Harare Zimbabwe in 1991 [36], to 148.7/100,000 py in Maputo Mozambique in 2006 [33] (**Table 3**). The random effect meta-analysis of population-based incidence rates was 112.94/100,000 py (95% CI = 90.7–135.17, $I^2 = 97.5\%$, p = 0.000) (**Figure 2**). The hospital-based meta-analysis was lower with a pooled estimate of 77.39/100,000 py (95% CI = 51.31–103.48, $I^2 = 99.1\%$, p = 0.000) (**Figure 3**).There were 11studies (all population/community-based) reporting crude prevalences of stroke survivors with prevalence rates ranging from 15/100,000 population in Ethiopia in 1988 [23], to 963/100,000 population in 2010 [28] (**Table 4**). Random effect meta-analysis yielded a pooled prevalence rate of 387.93/100,000 population (95% CI = 284.16–491.70, $I^2 = 98.8\%$, p = 0.000) (**Figure 4**). A Tanzanian study reported a prevalence of 2300/100,000 among people aged 70 years above in Hai district in 2010 [24], this was not included in the meta-analysis as other studies were mostly based on the general population with mean age ranging between 50 and 60 years (**Table 4**).

Modelled estimates of stroke incidence and prevalence rates in Africa

Based on the UN population demographics and bubble graphs derived from all data points, incident cases and number of stroke survivors were estimated for the year 2009, which was our estimated median year of study.

There were over 483 thousand new cases of stroke in Africa in 2009 among people aged 15 years or more equivalent to 81.2 (13.2–94.9)/100,000 py, with about 305 thousand and over 178 thousand new cases of stroke equivalent to 103.3 (20.7–109.2)/100,000 py and 59.5 (6.9–84.3)/100,000 py among men and women, respectively (**Table 5** and **Figure 5**). Comparable figures for the year 2010 and 2013 based on the same incidence rates would amount to 496 (80.6–579.7) and 535 (87.0–625.3) thousand new stroke cases respectively, suggesting an increase of 10.8% between 2009 and 2013 that is attributable to growth and ageing of the African population alone.

The estimated number of stroke survivors in Africa in 2009 was 1.89 million among people aged 15 years or more with a prevalence of 317.3 (314.0–748.2)/100000 population. There were about 990 thousand and 898 thousand stroke survivors equivalent to 335.5 (302.3–702.7)/100,000 and 299.3 (268.4–579.0)/100,000 among men and women, respectively (**Table 6**

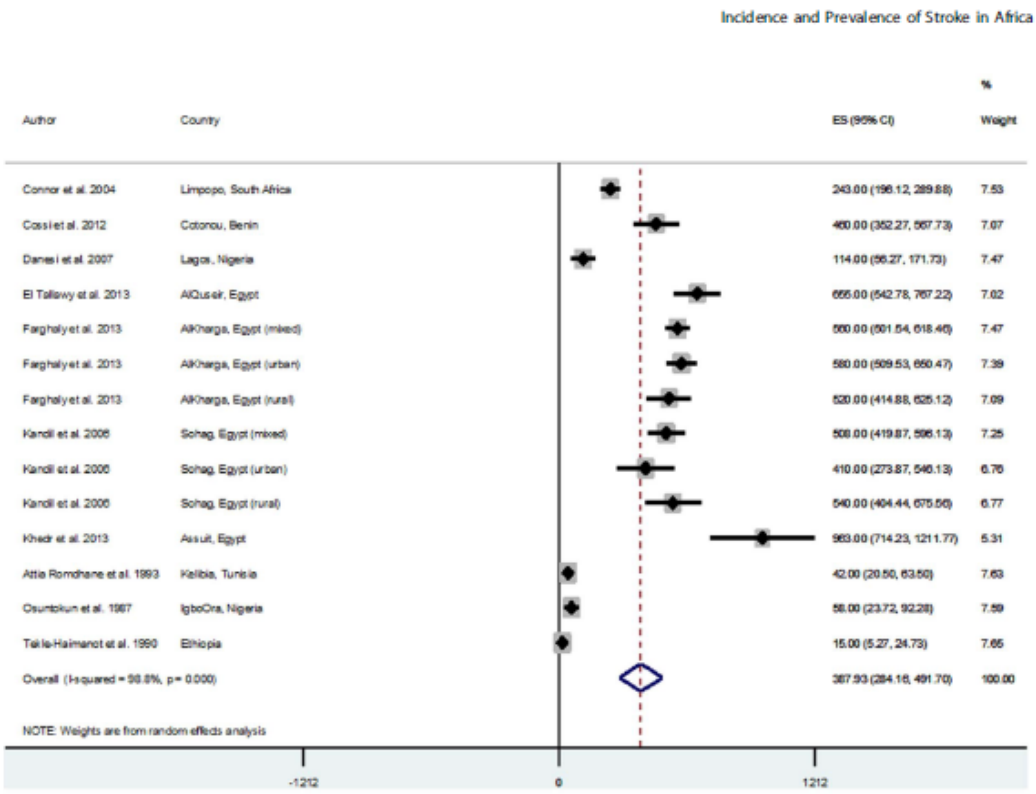

Figure 4. Pooled crude prevalence rates of stroke survivors from population-based studies.
doi:10.1371/journal.pone.0100724.g004

and **Figure 6**). Based on the same prevalence rates, comparable figures for the year 2010 and 2013 would amount to 1.94 (1.90–4.57) and 2.09 (2.06–4.93) million stroke survivors respectively, also suggesting an increase of 9.6% between 2009 and 2013 that is attributable to growth and ageing of the African population alone.

Discussion

Some systematic reviews have been published on the burden of stroke in Africa but without a continent-wide estimate of stroke incidence and prevalence rates [7,42]. There are also global reviews of stroke with few studies on Africa population included [13,43,44]. For example, in a systematic review of 56 population-based studies globally, only one African site (Ibadan, Nigeria) was considered. The result from this survey may not necessarily reflect the overall burden of stroke in Africa [13]. However, to the best knowledge, this study provides the first continent-wide estimate of the incidence and prevalence rates of stroke in Africa. The estimates were strictly based on a simple statistical analysis with appropriate consideration of reported mean ages and sample sizes from individual studies. Moreover, having applied the UN population demographics in our final model, the current estimates fairly reflect the, albeit very limited, available published data on incidence and prevalence rates of stroke in Africa, and may help policymakers across several African countries institute effective public health response to the growing burden.

Generally, crude incidences of stroke from population/community based-studies were higher with the two low incidence rates recorded obtained from population-based stroke registries in Nigeria [38,40] (**Table 3**). Despite over 3 decades of potential improvement in stroke registration between the two studies (1975–2007), the low incidence rates may still be indicative of incompleteness of stroke registries in many Africa settings, and that data obtained from these registries may be unreliable and inappropriate for estimation of stroke burden. In contrast, in many high income countries where there is active registration of stroke cases, population-based stroke registries have been reliable sources of data for estimation of stroke incidences [7,45]. In this study, the pooled crude incidence rate from community-based studies was higher at 112.9 per 100,000 person years compared to 77.4 from hospital-based studies. The difference suggests a likely under-estimation of stroke incidences from hospital-based studies, which has also been observed by some studies, particularly due to the very few stroke cases presenting to standard health facilities [2]. The observed prevalence rates of stroke survivors were generally high (all prevalence studies were population-based) with a pooled crude prevalence rate of 387.9/100,000 population. The low prevalence rate recorded in Ethiopia in 1988 may not be unconnected with the high mortality rates from stroke, which has generally been reported in many parts of Africa [23,46]. Moreover, the Ethiopian study was broadly a survey of neurological disorders in the community, which could possibly

Table 3. Summary of data from studies reporting crude incidence of stroke.

Author	Year	Age (years)	Cases (All)	Sample size (All)	Incidence/100000 py (All)	Cases (Male)	Sample size (Male)	Incidence/100000 py (Men)	Cases (Female)	Sample size (Female)	Incidence/ 100000 py (Women)
POPULATION/COMMUNITY-BASED											
Danesi et al. 2013	2007	All	189	750000	25.2	118	417000	28.3	71	333000	21.3
El Tallawy et al. 2013	2012	20+	36	19848	181	21	9916	212	15	9932	150
Walker et al. 2010a	2006	All	453	159814	94.5	532	71916	1067	10	87898	76.7
Walker et al. 2010b	2006	All	183	56517	107.9	266	25433	1152	122	31084	99.7
Osuntokun et al. 1979	1975	All	318	1223077	26	229	538462	25	89	684615	13
Kandil et al. 2006a	1993	All	39	25000	180	21	21000	100	18	21176	85
Kandil et al. 2006b	1993	All	11	8464	150	7	7778	90	4	7547	53
Kandil et al. 2006c	1993	All	20	11228	210	9	9278	97	11	9244	119
Farghaly et al. 2013	2007	All	156	62583	250	86	32165	270	70	30418	230
HOSPITAL-BASED											
Ashok et al. 1986	1984	15+	329	518745	63	184	267590	69	145	251155	58
Damasceno et al. 2010	2006	15+	651	437794	148.7	342	197007	1736	309	240787	128.3
El Zunni et al. 1995	1993	15+	921	1918750	48	379	1196154	52	322	722596	42
Matenga. 1997	1991	All	273	889250	30.7	142	478114	297	131	411136	32
Rosman 1986	1985	20+	116	114931	101	65	60343	108	51	54588	93

Walker et al. 2010a: Hai district (rural setting), Walker et al. 2010b: Dares Salaam district (urban setting).
doi:10.1371/journal.pone.0100724.t003

Table 4. Summary of data from studies reporting crude prevalence of stroke survivors (all population/community-based).

Author, year	Year	Age (years)	Cases (All)	Sample size (All)	Prevalence/100000 (All)	Cases (Men)	Sample size (Men)	Prevalence/100000 (Men)	Cases (Women)	Sample size (Female)	Prevalence/100000 (Men)
Connor et al, 2004	2002	15+	103	42378	243	37	20042	185	66	22336	296
Cossi et al. 2012	2009	15+	70	15155	460	38	6293	610	32	8862	360
Danesi et al. 2007	2006	All	15	13127	114	11	7295	151	4	5832	69
Dewhurst et al. 2013*	2010	70+	51	2232	2300	29	976	2971	22	1256	1752
El Tallawy et al. 2013	2012	All	130	19848	655	85	9916	860	48	9932	480
Farghaly et al. 2013a	2009	All	351	62583	560	196	32165	610	155	30418	510
Farghaly et al. 2013b	2009	All	257	44600	580	142	22908	620	115	21692	530
Farghaly et al. 2013c	2009	All	94	17983	520	54	9257	580	40	8726	458
Kandil et al. 2006a	1993	All	127	25000	508	65	12500	520	62	12500	490
Kandil et al. 2006b	1993	All	35	8464	410	20	4348	460	15	4116	470
Kandil et al. 2006c	1993	All	61	11228	540	29	5686	510	32	5542	570
Khedr et al. 2013	2010	All	57	5920	963	36	3066	1174	21	2854	736
Attia Romdhane et al. 1993	1985	All	15	34874	42	-	-	-	-	-	-
Osuntokun et al. 1987	1962	All	11	18954	58	-	-	-	-	-	-
Takle-Haimanot et al. 1990	1988	20-85	9	60820	15	-	-	-	-	-	-

*not included in meta-analysis, a: mixed setting, b: urban setting, c: rural setting.
doi:10.1371/journal.pone.0100724.t004

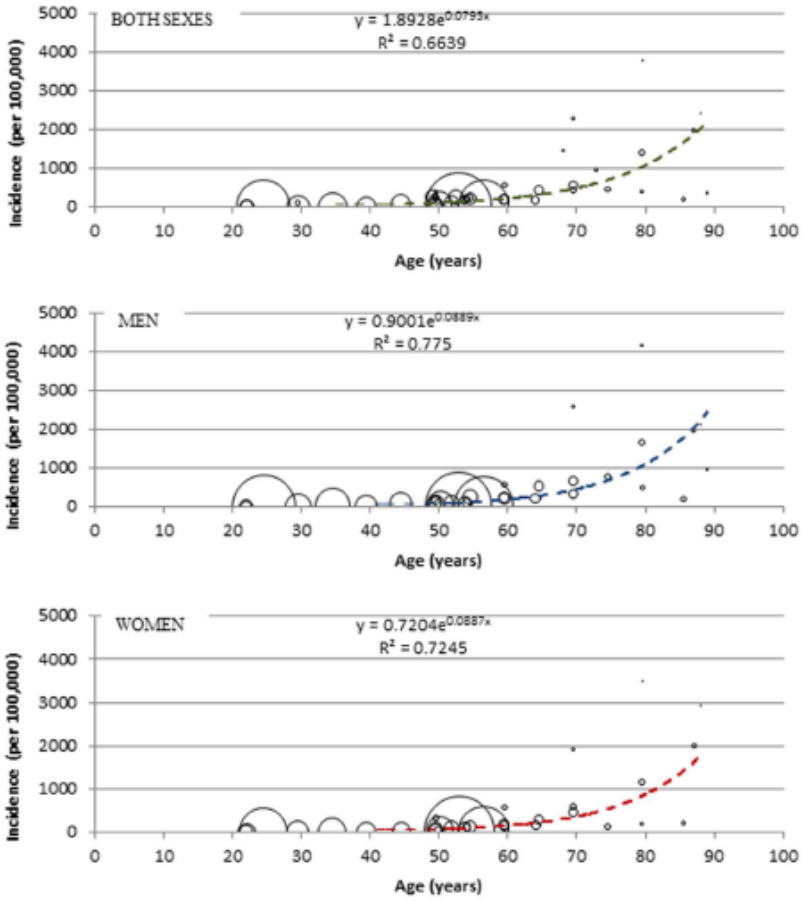

Figure 5. Bubble graph showing relationship between age and crude incidence of stroke, with size of bubble corresponding to sample size.
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imply that active case recognition of specific stroke cases may be less rigorous.

The modelling showed a rising incidence and prevalence rates of stroke with increasing age and higher figures recorded among men, which is in keeping with several research findings on stroke burden [24]. Over 483 thousand new cases of stroke with an incidence rate of 81.2/100,000 py (men 103.3, women 59.5), and about 1.89 million stroke survivors with a prevalence rate of 317.3/100000 population (men 335.5, women 299.3), both among people aged 15 years or more were estimated in 2009. A report in 2004 suggested that that about 8% of all first-ever strokes (about 5 million) occurred in Africa and 5% of over 30 million stroke survivors worldwide were in Africa [5,11], and this amounts to about 400 thousand new stroke cases and 1.5 million stroke survivors. A systematic review in sub-Saharan Africa on studies published between 1966–2006 showed age-standardized prevalence rates of 114–315/100,000 populations and 154–281/100,000 population among men and women, respectively [7]. Another review in 2006 showed that the prevalence of stroke survivors ranges from 200–300/100,000 population in sub-Saharan Africa, and incidence rates ranges from 15–68/100,000 py [42]. These figures are comparable with the current estimates, which further underpins a near representation of the burden of stroke in Africa. The minor differences may probably be due to the study periods, age groups, fewer data-points, focus on sub-Saharan Africa, and the fact that these were largely qualitative reviews and not based on a detailed statistical synthesis. However, according to the 2014 GBD estimates by Feigin and colleagues, over a 100% increase in the total number of new stroke cases and stroke survivors was recorded between 1990 and 2010 in LMIC, with an estimated incidence rate of 281.1/100,000 py and prevalence rate of 393.4/100,000 population in 2010 [1]. While it is understandable that not all LMIC have contextual similarities with African countries and direct comparisons may be inappropriate, it may however still be logical to conclude that the estimates from this study reflect the current stroke burden in many LMIC.

Table 5. Estimated new stroke cases and incidence rates in Africa in 2009 (estimates derived from bubble graph model and United Nations population figures).

Age (years)	Both sexes		Men		Women	
	Incidence (per 100,000 py) $=1.8928e^{0.079x}$	Stroke cases (000)	Incidence (per 100,000 py) $=0.9001e^{0.0869x}$	Stroke cases (000)	Incidence (per 100,000 py) $=0.7204e^{0.0887x}$	Stroke cases (000)
15–19	7.3	7.744	4.1	6.028	3.3	1.715
20–24	10.8	10.312	6.4	7.910	5.1	2.402
25–29	16.1	13.131	9.9	9.919	7.9	3.212
30–34	23.9	16.034	15.5	11.933	12.3	4.101
35–39	35.6	19.141	24.1	14.009	19.2	5.132
40–44	52.9	23.261	37.7	16.668	29.9	6.593
45–49	78.7	29.061	58.7	20.316	46.6	8.744
50–54	116.9	36.059	91.6	24.532	72.6	11.527
55–59	173.8	43.290	142.9	28.622	113.1	14.668
60–64	258.4	50.181	222.9	32.166	176.2	18.016
65–69	384.2	54.939	347.6	33.881	274.5	21.058
70–74	571.2	57.775	542.2	34.087	427.7	23.688
75–79	849.1	52.338	845.6	29.437	666.4	22.901
80+	1601.3	69.783	1722.0	35.059	1355.0	34.724
Total 15+	81.2 (13.2–94.9)	483.050	103.3 (20.7–109.2)	304.567	59.5 (6.9–84.3)	178.482

py: person years, x = midpoint of age group.
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While this study aimed to provide an evidence-based continent-wide estimation of stroke incidence and prevalence rates in Africa through simple statistical analysis, the study has some important limitations. In particular the low research output and quality of selected studies from Africa constrained the overall analysis. There were 19 studies covering only 10 countries in Africa with an overall sample size of over 6.3 million. Moreover, stroke case ascertainment were not well defined across some studies, and this has been documented in some reviews [45]. Due to these limited data and with some full texts assessed showing evidence of a detailed epidemiological exercise, an inclusion of some of these studies in our final analysis was allowed. In addition, some reported stroke incidence data were based on both first stroke and recurrent stroke events, and not all reported prevalence rates were strictly based on stroke survivors. However, having ensured all studies showed evidence of a degree of epidemiological survey rigour, and all extracted data points included in our modelling (refer to **Table 2**, and **Table S3** in **File S1**), the current estimates could still give a near representation of the burden of stroke in Africa.

Public health response to stroke in Africa

The prevention of stroke and many non-communicable diseases in Africa has been affected mainly by weak health systems and poor government response [46]. To date, the priorities of many African countries remain infectious diseases: mainly HIV/AIDS, malaria and tuberculosis [3,47], despite the availability of affordable and cost effective stroke prevention initiatives [48,49]. For example, Walker and colleagues reported that African countries do not have national strategies to address smoking, alcohol, physical inactivity and unhealthy diets including reducing salt and fat contents of processed foods [48]; and stroke units, where the awareness on these risk factors could have been raised, are rarely available [12,50]. The INTERSTROKE study findings show that hypertension is the main risk factor of all stroke subtypes with odds of about 2.64 [8], this is more prominent among young Africans who present with stroke unaware of their high blood pressure status [15]. Truelsen argues that the prevalence of stroke in Africa might increase due to substantial changes in major stroke risk factors in the presence of a biased focus on the prevention and control of infectious diseases, at the expense of many NCDs [51].

The diagnosis of stroke in many African settings remain a huge challenge [42]. Some hospital surveys in sub-Saharan Africa have shown that CT scans are only conducted on less than half of patients presenting with stroke, and this is mainly among those that can afford it [42,52]. In fact, experts have reported that the unavailability and/or high costs of cranial CT imaging in many parts of Africa have limited information on the pathologic profiles of different stroke types in the continent, with this often affecting the diagnosis, treatment and the overall management of the disease [52]. Reports further show that in some areas with better population-wide access to CT scans, as the case in Tanzania, Ghana, and the Medical University of Southern African (MEDUNSA) Stroke Data Bank (MSDB), there have been improvements in diagnosis of stroke, with varying cases of ischaemic and haemorrhagic strokes reported [53–55]. Moreover, the challenges of appropriately distinguishing first from recurrent stroke episodes have also affected stroke case ascertainment, especially during epidemiological surveys [7] Neurologists have noted the importance of proper planning during community surveys, active registration and follow-up of new stroke cases identified, and training and re-training of health workers on stroke diagnosis [17]; arguing that the absence of these in many African settings have resulted in increased number of stroke cases in the community who have never had contact with standard health facilities, and inability to categorize these as first or recurrent strokes, including relating such existing stroke cases to a particular period during surveys [7,17].

As noted earlier, a systematic review has suggested that income is a strong predictor of stroke risk and fatalities [6]. For example, the average cost of a cranial CT in Ugandan was approximately

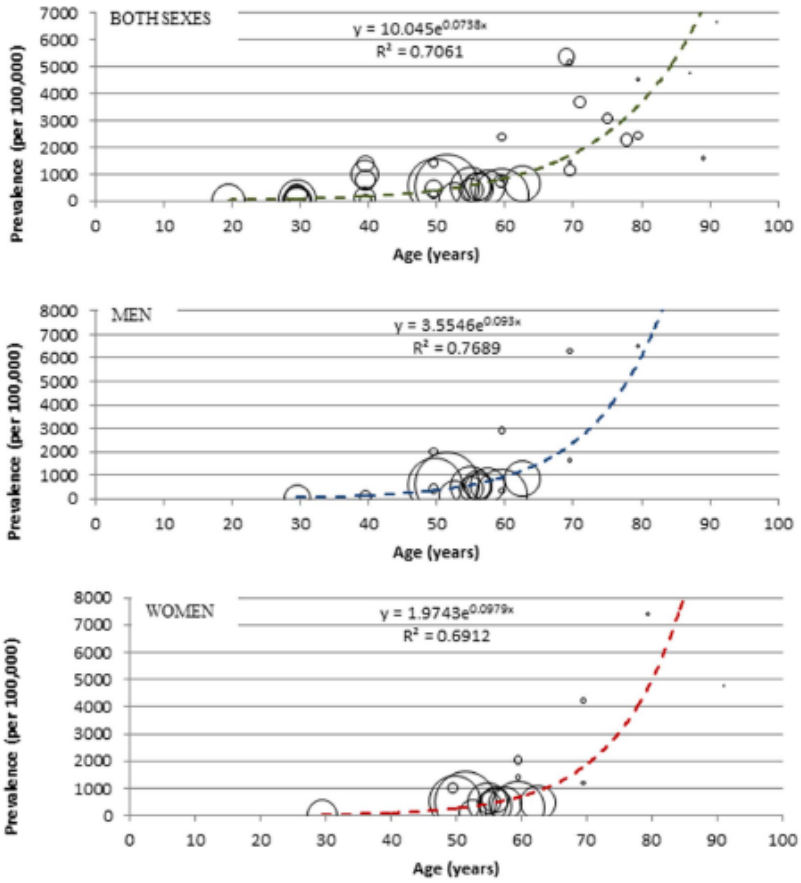

Figure 6. Bubble graph showing relationship between age and crude prevalence of stroke survivors, with size of bubble corresponding to sample size.
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$60 USD between 2000 and 2010 [2]. This is expensive in most African population groups where many still live below the poverty index of less than $1.25/day [56]. The high cost of health services in the absence of an effective health insurance schemes and adequate resources allocated for stroke prevention and management has affected healthcare seeking behaviour in some African settings [7,57]. Many stroke patients have been managed at home due to lack of hospital funds, with only few presenting to standard health facilities several days after the onset of symptoms having tried low-priced under-resourced clinics [2]. For those who manage to get to standard health facilities, there are also challenges arising from poor quality of care, as several studies have reported massive gaps exist in the management of acute stroke in Africa compared to many high income countries [58,59].

The unavailability of data with low research output has been a major setback in the management of stroke in Africa [51]. Experts have reported that reliable data from which evidence-based policy decisions can be made are sparse in Africa [60]. Many have argued that no study in Africa can be regarded as an ideal stroke study [17], adding that there were no proper stroke registries and demographic health surveys which invariably limit active registration, follow-up of cases and conduct of community-based studies [45]. Based on the current findings, hospital-based studies and door-to-door surveys were mainly conducted in Africa and despite the rigour of these few epidemiological surveys, gaps have been identified with regards to case ascertainment and study protocols [46].

Our findings suggest an increasing burden of stroke in Africa. However, with the current low availability of data, there is still need for more research on stroke, and related vascular disease risk factors to appropriately quantify this burden. An investment in research capacity, basically to conduct and find higher quality research may help raise awareness on stroke burden in Africa. An awareness and fair understanding of stroke burden and disease pattern in Africa may further prompt appropriate policy response and scale up current intervention programmes.

Table 6. Estimated number of stroke survivors and prevalence in Africa in 2009 (estimates derived from bubble graph model and United Nations population figures).

Age (years)	Both sexes		Men		Women	
	Prevalence (per 100,000) $=10.045e^{0.0718x}$	Stroke cases (000)	Prevalence (per 100,000) $=3.5546e^{0.0982x}$	Stroke cases (000)	Prevalence (per 100,000) $=1.9743e^{0.0979x}$	Stroke cases (000)
15–19	35.2	14.747	17.3	9.250	10.4	5.497
20–24	50.9	21.209	27.5	13.149	17.0	8.060
25–29	73.8	29.183	43.9	17.899	27.8	11.284
30–34	106.6	38.546	69.7	23.461	45.3	15.085
35–39	154.1	49.752	110.9	29.985	73.9	19.768
40–44	222.9	65.282	176.7	38.691	120.5	26.591
45–49	322.4	88.022	281.3	51.095	196.7	36.927
50–54	466.2	117.911	447.8	66.938	320.9	50.973
55–59	674.3	152.945	712.8	85.030	523.5	67.914
60–64	975.2	191.641	1134.8	104.301	854.1	87.341
65–69	1410.5	226.648	1806.7	119.754	1393.4	106.894
70–74	2039.9	257.559	2876.2	131.654	2273.3	125.905
75–79	2950.3	252.359	4579.0	124.904	3708.9	127.455
80+	5324.5	381.003	9635.8	172.991	8116.9	208.012
Total 15+	317.3 (314.0–748.2)	1886.806	335.5 (302.3–704.7)	989.099	299.3 (268.4–579.0)	897.708

x = midpoint of age group.

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Supporting Information

File S1 **Table S1.** Search terms (EMBASE). **Table S2.** Search terms (Global Health). **Table S3.** All data points employed in modelling.
(DOC)

Checklist S1 PRISMA Checklist.
(DOC)

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Author Contributions

Conceived and designed the experiments: DA. Performed the experiments: DA. Analyzed the data: DA. Contributed reagents/materials/analysis tools: DA. Wrote the paper: DA.

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Estimating the incidence of colorectal cancer in Sub–Saharan Africa: A systematic analysis

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Background Nearly two–thirds of annual mortality worldwide is attributable to non–communicable diseases (NCDs), with 70% estimated to occur in low– and middle–income countries (LMIC). Colorectal cancer (CRC) accounts for over 600 000 deaths annually, but data concerning cancer rates in LMIC is very poor. This study analyses the data available to produce an estimate of the incidence of colorectal cancer in Sub–Saharan Africa (SSA).

Methods Data for this analysis came from two main sources: a systematic search of Medline, EMBASE and Global Health which found 15 published data sets, and an additional 42 unpublished data sets which were sourced from the IARC and individual cancer registries. Data for case rates by age and sex, as well as population denominators were extracted and analysed to produce an estimate of incidence.

Results: The crude incidence of CRC in SSA for both sexes was found to be 4.04 per 100 000 population (4.38 for men and 3.69 for women). Incidence increased with age with the highest rates in Southern Africa, particularly in South Africa. The rates of CRC in SSA were much lower than those reported for high–income countries.

Conclusion Few health services in SSA are equipped to provide timely diagnosis and treatment of cancer in SSA. In addition, data collection systems are weak, meaning that the available statistics may underestimate the burden of disease. In order to improve health care services it is vital that accurate measurements of disease burden are available to policy makers.

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In 2008 cancer was the leading cause of mortality worldwide, responsible for the deaths of an estimated 7.6 million people [1]. Colorectal cancer (CRC) accounted for over 600 000 of those deaths, with 70% occurring in low– and middle–income countries [1,2]. With the emergence of non–communicable diseases (NCD) in countries where traditionally the biggest problem were infections, it is estimated that, by 2030, cancer will become the cause of over 13 million deaths a year [3]. While rates of infectious diseases typically decrease with the economic growth of a country, rates of NCD do not appear to decrease until high levels of education and lit-

eracy are reached [2]. The increasing prevalence of NCD is also having serious economic impact on health systems around the world, with the cost of long–term treatment for chronic conditions unsustainable in many health systems [3]. NCDs are heavily involved in the vicious cycle of health and poverty, where poor health results in loss of income, which in turn results in inability to pay for health care or maintain a healthy lifestyle [4]. Many NCDs result in chronic conditions requiring long–term medical expenditures and ongoing loss of income owing to ill health [5].

Low– and middle–income countries (LMICs) carry the majority of the burden of NCDs both in terms of incidence and mortality [6]. The rates of cancer are dramatically increasing partly because of the ageing population, and partly due to the rapid 'globalisation' and the adoption of the associated risk factors within these populations [7]. These risk factors include physical inactivity, smoking and alcohol consumption and poor nutrition [8]. A recent study found that over half of people aged 50 or over in SSA possessed at least 2 of the risk factors associated with NCDs [7].

Cancer registries cover less than 25% of the world's population. It is estimated that this proportion would reduce to 11% if only data of good quality is included [8]. The WHO collects data on cancer deaths from cancer registries around the world (**Box 1**) and produces estimates of the global and regional burden of cancer [14]. The International Agency for Research on Cancer (IARC) also publishes sets of estimates of global incidence and mortality through the GLOBOCAN project, the most recent from 2008 [15]. This data indicates that colorectal cancer (CRC) is the 5th most common cancer in SSA [15].

Although the reliability of the information provided in cancer registries, especially in SSA, is open to question, the registries remain one of the very few sources of data on cancer and therefore are the closest we can get to an estimate of the burden [8]. The size of the population denominator and the accuracy of the data can vary greatly between these sources, with only 23 of the 47 SSA countries having a formal registration system for cancer [16]. Many of these registries only cover small regions, often cities, within a country. Typically, the few rural registries indicate a much lower incidence of cancer than urban registries. Given that the majority of accessible data comes from urban registries, where only 40% of the population live and with higher risk factors, the estimates may be exaggerated [17] or gravely under–representative of rural areas.

Although the number of cases of CRC in SSA is thought to be very low in comparison to those diagnosed in the Western world (**Box 2**), it constitutes a significant proportion of the cancers in this region [24]. The aims of this study were to contribute to improving the evidence on the burden or NCDs in LMICs, by reviewing the evidence from the published literature (found through systematic review) and unpublished data on cancer registries to assess the burden of CRC in SSA. We also aimed to explore the quality and availability of data and to make suggestions for research and public health policy priorities to improve control of CRC in SSA.

Box 1 Non–communicable diseases and the global health agenda

In recent decades the focus of international health organisations for the developing world has been communicable diseases. As a result huge sums of money and political attention have been dedicated specifically to HIV/AIDS, malaria and tuberculosis. However, NCD are now a significant barrier to reaching some of the Millennium Development Goals (MDGs), which focus primarily on reducing infectious diseases [5].

In 2000, the resolution "Prevention and Control on Non–Communicable Diseases" was adopted by WHO member states at the World Health Assembly [9]. This resolution had three main aims:

1. Examine the major risk factors associated with NCDs
2. Introduce health promotion programs aiming to minimize the risk factors
3. Improve access to health care

Since this initial commitment to reducing the burden of disease caused by NCDs the World Health Assembly has also endorsed the Global Strategy on Diet and Physical Activity and Health [10,11], and the Framework Convention for Tobacco Control [12].

The UN high–level meeting on non–communicable diseases in 2011 recognised four major conditions that had previously been neglected by the international health community; cardiovascular disease, chronic respiratory diseases, diabetes and cancer [4,13].

METHODS

The data in this review came from cancer registries, and were identified through two main sources – a systematic review of the published literature and an analysis of the unpublished cancer registry data, as shown in **Figure 1**.

Search strategy for systematic analysis and data extraction

A systematic analysis of published literature on public domain was carried out using the databases Medline, Embase and Global Health. The search used both Medical Subject Headings (MeSH) and keywords as well as the individual countries in Sub–Saharan Africa. Search terms for Medline are outlined in **Table 1** and were modified where necessary for the other databases. Final searches were completed on 13 January 2012. All references found in the initial searches were exported to Refworks.

Box 2 Colorectal cancer and public health

Commonly CRC develops from adenomatous, colonic polyps with 65% in the rectosigmoid and 15% in the ascending colon or caecum [18]. Spread of the cancer is typically through the bowel wall and, in cases of rectal carcinoma, may invade the abdominal walls or pelvic viscera. Lymphatic invasion through the systemic or portal circulation is common with the liver and lungs as secondary sites [19]. The progression from adenoma to carcinoma is a well–documented process involving mutations in a number of genes such as APC (adenomatous polyposis coli), DCC, k–ras and p53 [18,20].

Approximately 80% of CRC is caused by environmental factors such as physical inactivity, smoking, alcohol and poor diet [21]. Nutrition is thought to be a major contributing factor to the differences in incidence of CRC between developing and developed countries. Western diets, typically high in fibre, increase faecal bulk, reducing transit time and resulting in a higher risk of developing malignancy [21]. The other 10% of CRC is caused by genetic mutations in two major pathways resulting in familial adenomatous polyposis (FAP) or hereditary non–polyposis colon cancer (HNPCC). Individuals with these diseases have a lifetime risk of CRC of up to 80% [21].

Screening for CRC is known to not only help detect the cancer in its early stages, and therefore improve chances of a curative treatment, but also to detect pre–cancerous lesions which, if removed successfully, can avoid more expensive and radical treatments [22]. Colorectal adenomas/polyps are extremely common in the Western world, occurring in approximately 20% of people over the age of 60 [21]. In the UK a national screening programmes for CRC have been launched, targeting those in the 50–74 age group. It is estimated that these interventions have resulted in a 16% reduction of mortality caused by CRC [23].

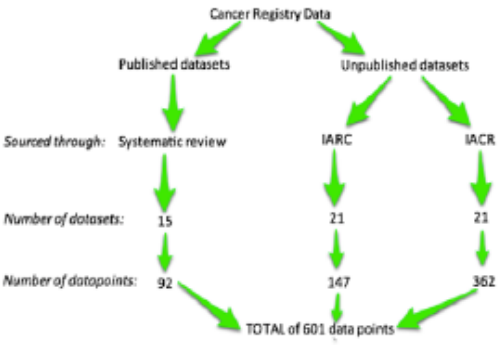

Figure 1 Sources of data.

Table 1 Search terms

1	prevalence/ or prevalen*.tw
2	mortality/ or mortal*.tw
3	global burden of disease/ or (disease adj3 burden*).tw
4	incidence/ or inciden*.tw
5	1 or 2 or 3 or 4
6	colorectal adenoma/ or CRC/ or colon cancer/ or rectum cancer/ or colorectal carcinoma/ or colorectal disease/
7	(bowel* or large intestine* or large bowel* or gut* or colorect* or colo* or rect*) adj3 maligna* or carcinoma* or neoplas* or cancer* or tumo* or polyp*).tw
8	6 or 7
9	SSA/ or (Africa* adj3 Sub–Sahara*).tw or (Africa* adj3 south* adj3 Sahara*).tw
10	exp Africa or central/ or exp Cameroon/ or exp Central African Republic/ or exp Chad/ or exp Congo/ or exp "Democratic Republic of the Congo"/ or exp Equatorial Guinea/ or exp Gabon/ or exp Africa, Eastern/ or exp Burundi/ or exp Djibouti/ or exp Eritrea/ or exp Ethiopia/ or exp Kenya/ or exp Rwanda/ or exp Somalia/ or exp Sudan/ or exp Tanzania/ or exp Uganda/ or exp Africa, Southern/ or exp Angola/ or exp Botswana/ or exp Lesotho/ or exp Malawi/ or exp Mozambique/ or exp Namibia/ or exp South Africa/ or exp Swaziland/ or exp Zambia/ or exp Zimbabwe/ or exp Africa, Western/ or exp Benin/ or exp Burkina Faso/ or exp Cape Verde/ or exp Cote D'Ivoire/ or exp Gambia/ or exp Ghana/ or exp Guinea/ or exp Guinea-Bissau/ or exp Liberia/ or exp Mali/ or exp Mauritania/ or exp Niger/ or exp Nigeria/ or exp Senegal/ or exp Sierra Leone/ or exp Togo/ or exp Comoros/ or exp Madagascar/ or exp Mauritius/ or exp Seychelles
11	9 or 10
12	5 and 8 and 11
13	Limit 13 to yr = 1980-current

The selection criteria used in screening relevant studies were: original studies, limited to post–1980, conducted in Sub–Saharan Africa as defined by the World Bank [25], involving any age–group or sex, with no restrictions on the language of publication. The retained studies were further evaluated for quality of design and methods; studies with clear case definition of CRC, a population denominator of more than 10 000, and numerical measure of disease frequency were included.

Given that the systematic review produced a limited number of relevant papers, we decided to search for other potential sources of information on CRC in SSA. It was predicted that many of the cancer registries in SSA might hold unpublished or more recent data that could be obtained through methods other than systematic review. The IARC Web site provided access to an unpublished document presenting the data from cancer registries across SSA. Further review of this paper showed that some of the data had already been used in published articles found through the systematic search. However, there were an additional 21 data sets that met the criteria for this review. Permission to use this further data for analysis in this review was sought from the IARC through the World Health Organization (WHO). This was granted and is presented in Online Sup-

plementary Document, where a sample of the data extracted from this IARC paper is also shown.

Contact details for the directors of cancer registries in SSA were provided on the IACR Web site [16]; they were contacted to investigate whether they had any unpublished data that could be included with permission. Of the 23 directors contacted, 11 replied. Two replies directed attention to the IARC document, mentioned above, that had the most recent data for their registries. Seven of the replies, although positive and encouraging, provided no additional data. The reply from Botswana contained data for CRC from 1998 to 2011. The reply from the South African national cancer registry provided details of their Web site which had extensive information on cases of CRC between 2000 and 2004 and population data for 2000–2002. Population estimates for 2003 and 2004 were obtained through the South African government statistics Web site [26]. This second additional source provided the current review with a further 21 datasets. Examples of the data received directly from cancer registries are presented in the Online Supplementary Document. Owing to the extensive data available for South Africa a separate analysis was carried out investigating incidence trends over a 5–year period for different racial groups [27-31]. All the unpublished cancer registry data, both from the IARC and the IACR, was screened using the same selection criteria employed in the systematic literature search to ensure that the data was of comparable quality.

The initial search of Medline, Embase and Global Health databases returned 3127 articles, after the removal of duplicates, as shown in Figure 2. Sixty–five articles were sourced for the full–text version, and of these, 15 were selected for inclusion in the review. The 50 articles considered irrelevant did not comply with the exclusion/inclusion criteria set for this review; however, some were retained for extra information, mainly in the discussion. The 15 relevant articles [10,20,32-42] were then supplemented by the 21 data sets secured with permission from the IARC [43,44] and the further 21 data sets which were received from the directors of the cancer registries through the IACR [16]. Six articles, which were not suitable for contribution to the estimates of incidence but were sourced for full–text copies, were retained for information on the biological characteristics of CRC diagnosed in SSA. Data from the articles was extracted and complied into spreadsheets in Microsoft Excel. Cases of CRC were separated into age groups and by sex where appropriate. Incidence estimates were either extracted from the included data sets or calculated using the data reported. All estimates were converted to incidence per 100 000 of population (in that sex and age group) per year to allow for direct comparison between results. Data from 6 additional articles, not used for calculating incidence, were extracted for more detailed information on the biological characteristics of CRC.

Case definition used in retained studies

The different definitions of CRC cancer used in the data sets are presented in Figure 3. The majority defined it based on the current International Classification of Diseases (ICD–10), as devised by the World Health Organisation [45]. Five data sets, the ones typically undertaken in the 1980s and early 1990s, defined CRC based on the earlier ICD–9. The remaining data sets (labelled 'other' in Figure 3) took retrospective data from cancer registries and did not give a specific definition of CRC. However, 20 of these came from the South Africa Cancer Registry and it would be reasonable to assume they may have used ICD–10. The International Classification of Diseases for Oncology (ICD–O) was also used in the diagnosis of CRC for nearly 60% of the data sets, with five using the 1st edition (ICD–O–1) and 28 using the 2nd edition (ICD–O–2).

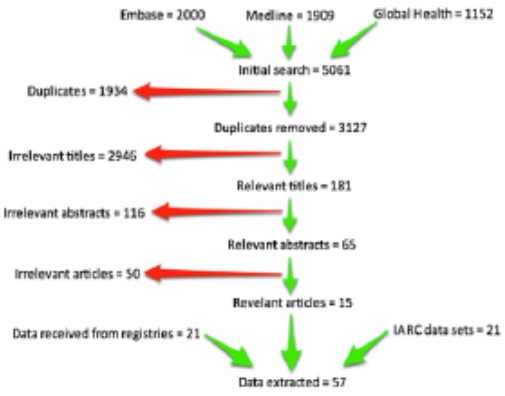

Figure 2 Search strategy.

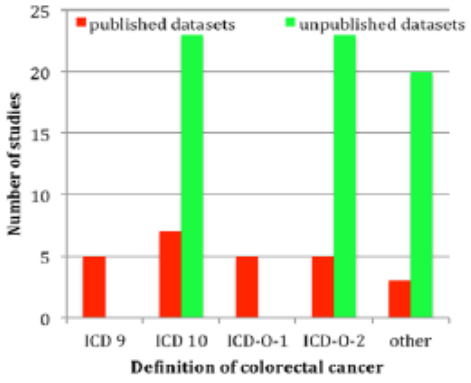

Figure 3 Definition of colorectal cancer in data sets. ICD – International Classification of Diseases (World Health Organisation).

Data analysis

There were a total of 57 data sets available from the published articles (identified by the systematic review) and the unpublished data from the cancer registries. This provided a total of 601 datapoints for the calculation of incidence. In this pooled series, 28 data sets contained statistics for the population of the area covered by the registry separated by age and sex. They also gave the raw data on the number of cases of CRC diagnosed over in given time period, also separated by age and sex. This allowed for a simple calculation of the incidence for each sex and age group. Five of the data sets did not contain information on the population denominator for each age group. In these cases the total population was either cited or could be calculated by working back from the reported incidence and cases of CRC. This number was then separated into age groups using total population data for the relevant year and country and adjusted to the size of the study population.

In 3 data sets which neither presented the population denominator, nor showed the number of cases of CRC by age group, the average age of the population (separated by sex) was calculated using UN ESA data for the relevant year and country [46]. This was then combined with the overall reported incidence of CRC by sex, calculated using the above method. A few data sets presented the number of cases separately for colon and rectal cancer. However, data for the two were combined to allow for easier comparison with other data sets. Tables were compiled using Microsoft Excel and contained all the information extracted from the data sets (see Online Supplementary Document for further details).

The average age was calculated as the mean age of each age range as reported in the data sets. This resulted in a total of 601 data points of incidence against age, separated by sex. Graphs containing the 601 data points of incidence by age for male, female and both sexes were used to separate incidence estimates into age groups. The age ranges were based on the groups used by the data sets from the IARC. From this, the minimum, maximum, lower quartile, upper quartile and median could be calculated for each age group. This data was used to create box–and–whiskers plots of the collected information. The median values of incidence by age group were then combined with the UN ESA statistics for the total population of SSA to calculate the number of new cases in a year. Examples of this are presented in Online Supplementary Document along with the all–age data that were calculated by each data set.

Moreover, twenty data sets from the South African cancer registry were used to conduct a separate sub–analysis of time trends in incidence of CRC in South Africa from 2000 to 2004. These papers also provided valuable data on the relationship between ethnic group and incidence of CRC. Furthermore, data from 6 articles excluded from the systematic review nevertheless had useful background information on three aspects of CRC: presenting symptoms, anatomical site of tumour and Duke's Stage of cancer at diagnosis. These papers provided percentage distributions, from which the averages could be calculated.

To ensure that the data was extracted accurately from both the published and unpublished data sets, one author (AG) performed a second data extraction on a random selection of 8 data sets. The number of cases of CRC as well as the underlying population denominator was extracted again. This represented 112 of the total 601 data points, and found that 100% of the data was the same. Therefore it was concluded that the accuracy of the data extraction was high.

RESULTS

The data sets showed a wide geographical distribution in SSA, as shown in Figure 4. Approximately 5% of data sets came from Central Africa, and 15%, 55% and 25% from West, Southern and East Africa respectively. However, clusters of data sets came from larger cities or countries known to conduct high levels of research. All data sets reported cancers from all age groups. The average size of the population denominator covered by the cancer registries was approximately 2 million. Ninety percent of the data sets reported data from population–based cancer registries, the remaining six were hospital–based. Some of the national cancer registries combined data from regional hospitals and smaller registries across the country. Figure 5 shows the distribution of active data sets over time. The majority were

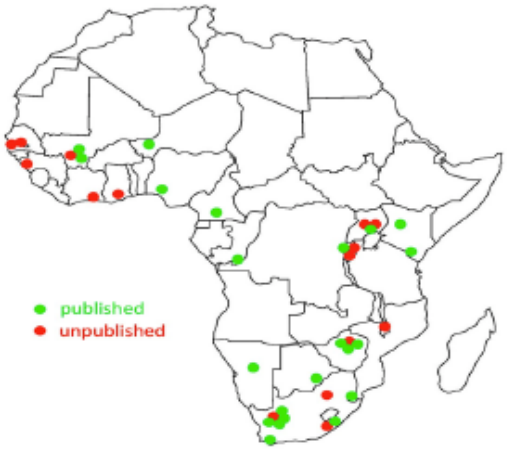

Figure 4 Geographical distribution of data sets. Additional 20 unpublished data sets came from South African Cancer Registry (not shown).

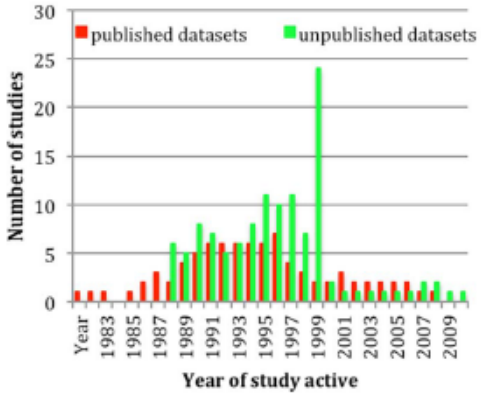

Figure 5 Active data sets active in study years.

conducted in the late 1990s to early 2000s with very little data available for the 1980s and a limited number from the last decade. As a result, any estimates produced by this review should be regarded as referring to 2000.

Incidence of CRC in Sub–Saharan Africa

Figure 6 show the distribution of incidence by age, calculated from all 57 data sets, producing 601 data points. The age–related distribution of incidence shows the predicted pattern, based on the biology of CRC, of substantial increase with age. It can also be noted that the calculated incidences are much higher in males than females. There were large variations in reported all–age incidence, owing to CRC being predominantly a disease of the elderly. As such, incidences were separated into age groups that were decided based on the ranges used by the primary data sources. They were selected to ensure that the majority of data points were the median in the ranges chosen. Figure 7 shows the box–and–whisker plots produced from allocating the individual data points into age groups. The values used for these graphs are presented in Online Supplementary Document. The median values of incidence for males, females and both sexes by age group are shown in Table 2. As expected, the incidence increases with age, with the incidence in people below 35 years being negligible. Again, it is also evident that the incidence of CRC is significantly higher in males than females.

Figure 8 shows the crude incidence of CRC in SSA by African sub–regions. The data used for these figures are presented in Online Supplementary Document. The crude incidence of CRC in SSA was found to be 4.04 cases per 100 000 population. This incidence was significantly higher in Southern Africa, which is discussed later in the text. The median incidence values calculated in Table 2 were

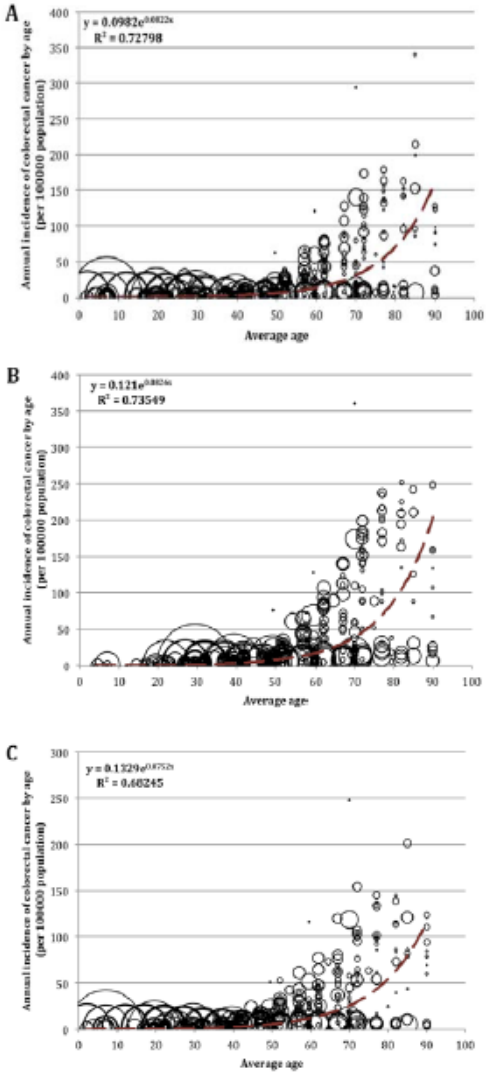

Figure 6 Incidence of colorectal cancer by age groups for both sexes (**A**), men (**B**) and women (**C**).

Table 2 Crude annual incidence of colorectal cancer in Sub–Saharan Africa (per 100 000 population)

	Age (years)							
	0–14	15–24	25–34	35–44	45–54	55–64	65–74	75+
Both sexes	0.00	0.26	1.15	3.48	8.72	22.11	34.37	86.87
Men	0.00	0.31	1.22	3.40	8.84	21.13	37.00	103.48
Women	0.00	0.10	0.91	2.91	8.09	15.65	23.48	71.36

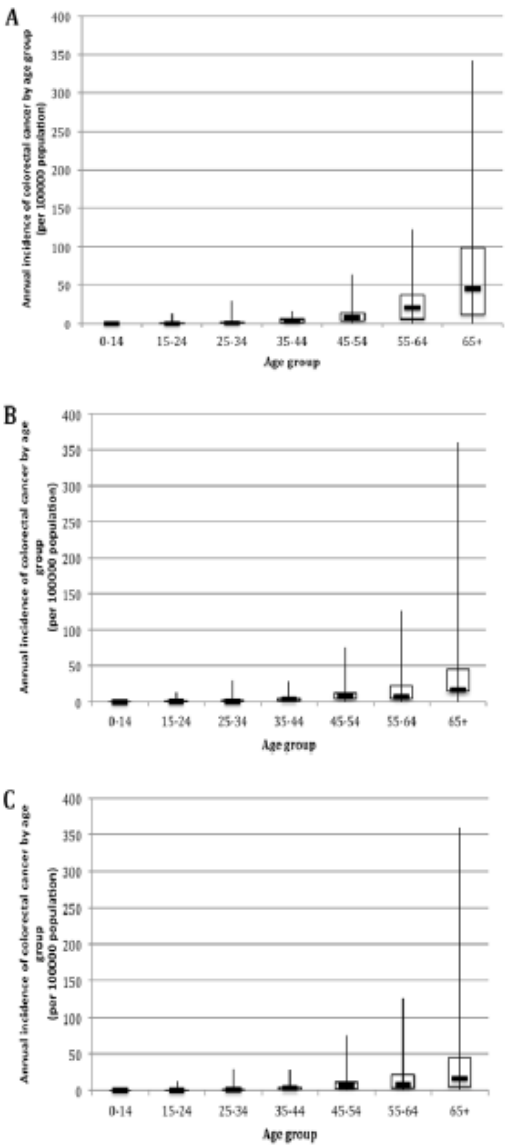

Figure 7 Crude incidence of colorectal cancer by age group for both sexes (**A**), men (**B**) and women (**C**).

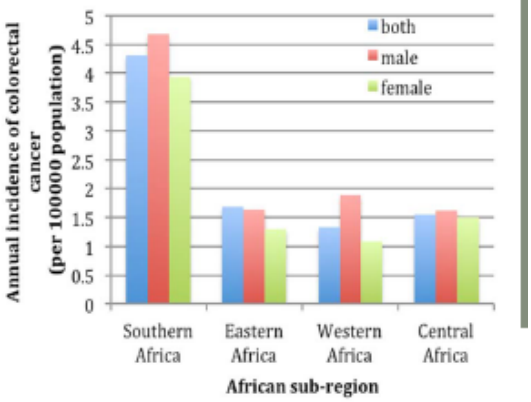

Figure 8 Annual crude incidence of colorectal cancer by African sub–region (per 100000 population).

combined with the UN ESA 2000 estimates for SSA. This produced Table 3 showing the estimated number of new cases of CRC reported in that year. The reason for using the 2000 population data are considered in the discussion section of this review. It is apparent that the majority of diagnoses of CRC occur in age groups older than 55 years, again with CRC more frequent in males than females. Table 4 shows a comparison of the estimates produced by this review and those from GLOBOCAN [44]. The estimates are very similar, with the minor difference perhaps explained by the predicted year of the estimates; this will be discussed later in this review.

Subsidiary information

Owing to the high standard of data available from the South African Cancer Registry for 2000–2004, a separate analysis was carried out to assess the relationship between incidence of CRC and ethnicity over time (Figure 9). Although the data refers to a relatively short time period, the differences in incidence between different ethnic groups can be observed very clearly. Two of the data sets in this review, with further six found through the systematic review, contained information on the nature of the cases of CRC diagnosed in SSA. Five papers contained information on the

Table 3 Annual number new cases of colorectal cancer in Sub–Saharan Africa in 2000

	Age (years)							
	0–14	15–24	25–34	35–44	45–54	55–64	65–74	75+
Both sexes	0	456	1428	2791	4651	7808	6732	1099
Men	0	267	762	1371	2294	3514	3321	3069
Women	0	67	565	1158	2216	2922	2492	1575

Table 4 Comparison of estimates of annual new cases of colorectal cancer in Sub–Saharan Africa

	Current review's estimate	GLOBOCAN estimate
Both sexes	23147	24711
Men	11300	13666
Women	9536	11045

GLOBOCAN – WHO project to provide contemporary estimates of the incidence of, mortality, prevalence and disability-adjusted life years (DALYs) from major type of cancers, at national level, for 184 countries of the world.

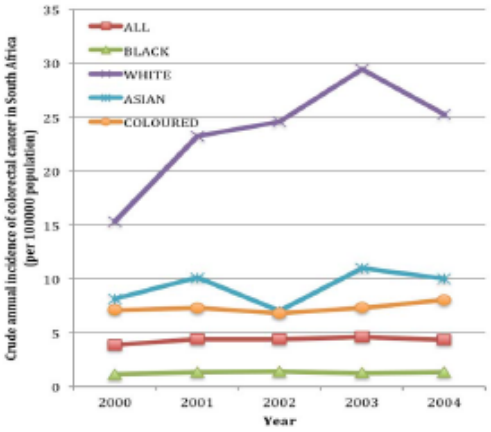

Figure 9 Crude incidence of colorectal cancer in South Africa (per 100 000 population) by ethnicity for 2000–2004.

anatomical sub–site of CRC, and the findings are presented in Figure 10. Although the percentage of cases in each anatomical location varied between the papers, all reported the rectum as the most common site, with one paper reporting this to include as high as 60% of cases. Data regarding the symptoms at presentation were obtained from five papers, shown in Figure 11. The most common presenting symptom was found to be bloody stool with nearly 57% of patients reporting this. It must be remembered that some patients may have recognised more than one of the symptoms listed. In addition, some patients may not have noticed less dramatic symptoms, such as altered bowel movements, until prompted by a medical professional. Figure 12 presents information from four papers that contained data on the Duke's Stage of the case of CRC diagnosed. It can clearly be seen that the majority of cases were diagnosed at Stage B, with very few at the first or last stage.

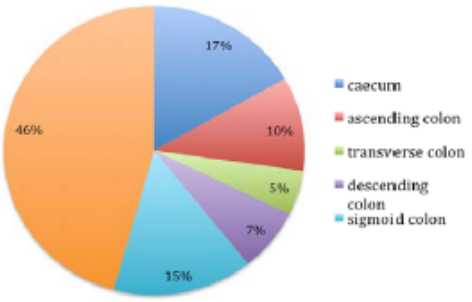

Figure 10 Colorectal cancer by anatomical tumour site.

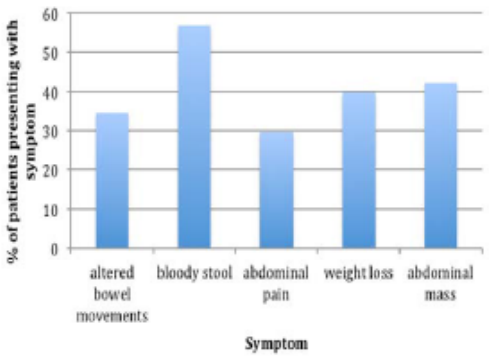

Figure 11 Presenting symptoms in colorectal cancer.

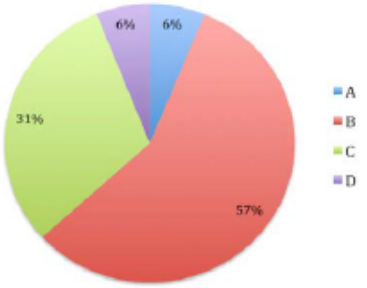

Figure 12 Duke's staging of the colorectal cancer.

DISCUSSION

This study found the incidence of CRC in SSA to be higher in males than females with the peak in the 75+ age group and a crude incidence of 4.04 per 100 000 population. On the basis of the incidence calculated by this review, it was estimated that there were about 23 000 new cases of CRC in 2000, with nearly 59% occurring in males. Based on the available evidence, the incidence of CRC in SSA appears to be much lower than in high–income countries. However, the trends associated with sex and age were very similar. The male:female ratio in the UK is estimated to be 1.26 while this review estimated the SSA ratio to be 1.19 [47]. One of the greatest concerns related to these overall conclusions may be that the incidence of CRC in Africa is systematically under–reported and that it is generally of poorer quality than in high income countries. However, the data from South Africa in the years 2000–2004 provide the best available evidence that the overall conclusions are likely to be true. This is because South Africa has registries of the highest qualities and its diverse demographic structure offers a direct comparison of the rates in different ethnic pop-

ulations. In South Africa, incidence is highest in whites, followed by the Asian and then coloured populations, with blacks having the lowest reported incidence [27-31].

This review also found that the major anatomical site of CRC was the rectum (in 46% of cases), followed by the caecum (17%). These trends are fairly similar to those found in the Western world. A study looking at anatomical sub–site of CRC in Europe found the most common sites to be rectum (31%), sigmoid colon (21%) and caecum (10%) [48]. Although the presenting symptoms reported by papers in this review were not very different from those elsewhere in the world, the signs associated with the more advanced stages of the disease, such as rectal bleeding, appear to be more common [49]. Moreover, this review found that a majority (57%) of cases of CRC were at Duke's Stage B at diagnosis, with very few cases being found at the most treatable Stage A. This does not support concerns that in Africa, because of less developed and less efficient health systems, cancer would generally be diagnosed at a later stage – at least it is not true for CRC and in registries that likely over-represent urban areas. However, this may also be due to lack of expert knowledge of the condition, leading to incorrect staging of tumours. This highlights the need for further research into this area in order to improve public health service provision.

In terms of the quality of primary data used in this study, there were two main sources of potential limitation: incomplete data and systematic bias. Although the problem of incomplete data was only encountered in 9 of the 57 data sets, it should not have affected the overall conclusions. Twenty–one of those data sets were obtained from direct contact with cancer registries in SSA. This review should not be affected by a major language bias, as data sets have been retrieved in all major languages used in Africa, including French and Dutch. It is also unlikely that this review is limited by the conventional form of publication bias, as unpublished registry data was also included. It is important to note that the latter may provide more recent data than that from published papers owing to the usual delay in the release of articles. The majority of data sets eligible for inclusion in this review contained data from the late 1990s and early 2000s. As such, any estimates produced by this review essentially refer to a mid–point of the year 2000, and are based on the correct population denominator from UN ESA. This was the best estimate that could be produced with the data available However, it is recognised that rates of NCDs are increasing in the developing world and therefore the estimates for 2000 are likely to be lower than the true current level.

This review made a comparison between the estimated number of new cases of CRC in Africa and estimates produced by GLOBOCAN [44]. Although it appears that this review underestimates the incidence in comparison to GLOBOCAN, it should be noted that there is an 8–year difference, with GLOBOCAN reporting the estimates for the year 2008. However, a short analysis of the data sources used by GLOBOCAN found that the majority of their data points also came from the 1990s. This probably explains the great similarity between the two estimates, which are very supportive of each other. However, because this review uses the same primary data with an additional 36 data sets it could be viewed as more comprehensive.

Finally, this review used information from 57 mutually exclusive cancer registry data sets, 15 of which came from articles published in peer–reviewed journals and 42 from unpublished data sources. The assumption is that the peer–reviewed articles would be of a higher quality so it was important to explore differentiating incidence across these two sources in a simple sensitivity analysis. The results are presented in **Table 5**. Although there are modest differences in incidence, this is partly driven by the inclusion of the South African data sets. The difference in incidence between published and unpublished data sets was significantly lower with the exclusion of South African data from both.

In terms of the validity and reliability of case definitions used to measure the frequency of CRC in the population in Africa, the current National Institute for Clinical Excellence (NICE) provides clinical guidelines that recommend the use of colonoscopy, biopsy, sigmoidoscopy, CT scan and barium enema in the diagnosis of CRC [50]. However, in many resource–poor settings, such as those found in a number of SSA countries, such extensive diagnostic tests are not feasible. Many registries only document histologically–diagnosed cancers, but even this is lacking in some areas [51]. This may result in the number of cases of CRC being underestimated in some settings. Another possible point of concern comes from the notion that some data sets included in this review did not specify whether ICD or another classification system was used as their case definition. Earlier versions of the ICD that preceded ICD–10 were recognized to be less specific [52]. This concern should be noted in regard to interpreting any fluctuations in the reports from cancer registries that were active over a long period of time. It is estimated that only 1% of the population of Africa are covered by cancer registries [53]. With limited resources and critically low numbers of health workers, the imple-

Table 5 Sensitivity analysis of published vs unpublished data sets

	Crude incidence of CRC/100000 population	
	Published data sets	Unpublished data sets
With South Africa	1.11	4.28
Without South Africa	1.07	2.05

mentation of a cancer registry has not been seen as a priority in tackling the burden of disease in many countries. However, accurate measurement of diseases is vital in achieving effective and efficient intervention programs [54].

Although data for 19 different countries in SSA was obtained, over 75% of the data points came from countries in Southern and Eastern Africa. These regions were found to have the highest incidences of CRC. Given that the majority of these data sets came from South Africa and Zimbabwe, it is important to recognise the differences in the population of these countries in comparison to the rest of SSA. These two countries had the highest incidence of CRC of the countries studied. South African law previously segregated its people into 4 ethnic categories; "Black", "Coloured" (mixed–race), "White" and "Asian/Indian". Although this law was abolished over 10 years ago, much of the population still identify themselves based on these groups and many epidemiology studies still separate the population in this way [55]. This can still be seen as evident in the data provided by the South African Cancer Registry for 2000–2004. Similarly, the data sets from Zimbabwe also separate their population into "African" and "European". This separation between ethnic groups allows for comparison between the groups, especially given the well–documented variation in incidence of CRC between white and black populations, which is consistently shown to be substantial.

South Africa is also known to have the highest numbers of people infected with HIV/AIDS of any country in Sub–Saharan Africa [56]. There is evidence to suggest an increased risk of developing CRC amongst HIV/AIDS infected populations, however the biological mechanism behind this is still poorly understood [57]. Karposi's sarcoma is strongly associated with HIV/AIDS infection and there are documented cases of involvement of the colorectum [58,59]. It is also possible that this may account for the higher incidence of CRC in South Africa. However, countries like Swaziland and Botswana, with higher percentages of HIV/AIDS infected populations had much lower incidence of CRC.

Ideally, cancer registries should be population–based, however, in developing countries, this is often not possible. Problems such as the limited health system infrastructure and cultural and religious obstacles in the reporting of diseases like cancer have contributed to the lack of routine data collection [54]. The alternative option of data collection through a hospital–based registry is better than no registry at all. This type of data will only cover people who have presented and been recognised as symptomatic at a local health facility, have been referred to centres where there are cancer services, and who can access these health care facilities, both physically and financially. However, it can still provide valuable information on cancer, particularly if adjustments can be made for selection biases in the population using the hospital. Because of this triaging system from primary to secondary care, those seeking medical attention are likely to be from higher socioeconomic backgrounds with higher levels of education and a greater awareness of the risk factors for developing diseases such as cancer. However, these people are also more likely to live a 'Westernised' lifestyle; increasing their risk of developing CRC. Hospital–based studies are also often based in urban areas where the risk profile is very different to those people living in rural areas. This highlights the need for national, population–based studies or more sophisticated data adjustments to ensure that any estimates produced are an accurate representation of the whole country.

To illustrate the difference between hospital–based and population–based cancer registries, a comparison of the crude incidence of CRC (per 100 000 population) is presented in Figure 13. Again, ideally a more sophisticated sub–group analysis would be undertaken to account for the influence of this apparent difference. Adjustments should be made allowing for the differences in the source of the data (published/unpublished), geographical coverage (particularly with reference to the dominance of South Africa) and the ethnic group of patients.

In many urban areas of SSA, there has been an increase in health risk behaviours associated with CRC, such as smoking, decreased physical activity, alcohol consumption and poor diet. There is also evidence of the increase in the health consequences of these behaviours, in terms of increased rates of obesity, diabetes and hypertension [51]. It is important that health education programs are set up to enable people to be more aware of the consequences of these unhealthy behaviours. Prevention is a more cost–effective and

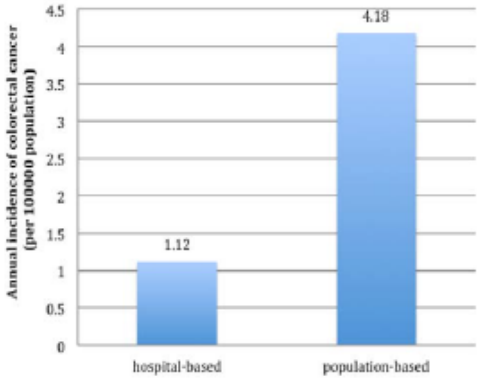

Figure 13 Comparison of incidence of colorectal cancer (per 100 000 population) in sub–Saharan Africa between hospital–based and population–based cancer registries.

long–term solution to dealing with the burden of cancer than treating the cases once diagnosed [60,61]. Although screening for CRC is thought to be cost–effective in high–income countries, whether this is the case in LMICs is debated. Implementing a screening program for CRC requires the purchase and maintenance of expensive equipment, skilled specialists and education of the public to maximise utilisation. Lambert et al. argue that this is not feasible in resource–poor settings like SSA [62]. However, with more accurate data from population–based studies it may be that the burden of disease attributable to CRC is greater than first thought. In this case, screening programmes, particularly if they are linked to a more generic family health programme engaging both men and women, may be a more cost-effective option to treating more advanced cancers.

In low–resource countries the national budget devoted to health systems is extremely low and as a consequence the public health service provision can be very weak [63]. This has led to the treatment options for patients with all forms of cancer including CRC in SSA being severely limited in comparison to patients in the Western world. For instance, a surgical procedure commonly performed in high–income world as a treatment, such as resection, was noted to only be attempted in very few countries that have specialist cancer hospitals and only in cases where the patients themselves were able to afford the cost of the procedure [24]. Cultural factors are also relevant to the acceptance of treatment, with some patients refusing to undergo surgery because of fear that a colostomy could result in rejection from their community [24,49]. It is estimated that only 18% of the need for radiation treatment in cancer patients is met in Africa as a whole, and this is likely to be even lower in the Sub–Saharan region [64]. Delays in seeking medical attention mean that for many patients with advanced stage of cancers palliative treatment was the only available option [49]. Follow–up of patients in all clinical settings is notoriously poor. One study reported that less that 30% of patients who received adjuvant treatment were seen again after six months. Although the reasons for this will be multifactorial, it was suggested that the treatment for many of these patients was unsuccessful and they had died [49].

In order to improve the volume and quality of information available on cancer in SSA there needs to be stronger investment in cancer registries. Being able to counter the arguments that it is not effective, efficient or ethical to invest scarce resources in setting–up cancer registries purely for epidemiological research purposes is important as such data sources will become an invaluable source of evidence and guidance for policy setting, programme implementation and improving practice.

In summary, this systematic analysis has highlighted the lack of data on CRC, mirroring the lack of data for all cancers in SSA. There is a notable lack of any recent published data. Greater use could be made of cancer registry data through direct contact and open access to their databases. All NCDs, including CRC, are increasing in low–income regions such as SSA. It is vital that the burden of disease attributable to this is accurately and regularly monitored. More information on the dynamics of this burden is also required, including who is affected, where and whether they have adequate access to treatment.

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ORIGINAL RESEARCH

An Estimate of the Prevalence of COPD in Africa: A Systematic Analysis

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Abstract

Background: **Chronic obstructive pulmonary disease (COPD) is among the leading causes of death globally, accounting for about 3 million deaths worldwide in 2011. We aimed to estimate the prevalence of COPD in Africa in the year 2010 to provide the information that could assist health policy in the region. *Methods:* We conducted a systematic review of Medline, EMBASE and Global Health for studies on COPD published between 1990 and 2012. We included original population based studies providing estimates of the prevalence of COPD. We considered the reported estimates in terms of the mean age of the sample, sex ratio, the year of study and the country of the study as possible covariates. Results from two different types of studies, i.e., based on spirometric and non-spirometric diagnosis of COPD, were further compared. The United Nation Population Division's population figures were used to estimate the number of COPD cases in the year 2010. *Results:* Our search returned 243 studies, from which only 13 met our selection criteria and only five were based on spirometry. The difference in the median prevalence of COPD in persons aged 40 years or older based on spirometry data (13.4%; IQR: 9.4%–22.1%) and non-spirometry data (4.0%; IQR: 2.1%–8.9%) was statistically significant ($p = 0.001$). There was no significant effect of the gender or the year of the study on the reported prevalence of COPD in either set of studies. The prevalence of COPD increased with age in spirometry-based studies ($p = 0.017$), which is a plausible finding suggesting internal consistency of spirometry-based estimates, while this trend was not observed in studies using other case definitions. When applied to the appropriate age group (40 years or more), which accounted for 196.4 million people in Africa in 2010, the estimated prevalence translates into 26.3 million (18.5–43.4 million) cases of COPD. Comparable figures for the year 2000 based on the same prevalence rates would amount to 20.0 million (14.1–33.1), suggesting an increase of 31.5% over a decade that is attributable to ageing of the African population alone. *Conclusion:* Our findings suggest that COPD is likely to already represent a very large public health problem in Africa. Moreover, rapidly ageing African population should expect a steady increase in the number of COPD cases in the next decade and beyond. The quantity and quality of available evidence does not match the size of the problem. There is a need for more research on COPD prevalence, but also incidence, mortality and risk factors in Africa. We hope this study will raise awareness of COPD in Africa and encourage further research.**

Keywords: Africa, chronic obstructive, COPD, chronic bronchitis, prevalence, pulmonary disease

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Introduction

The burden of non-communicable diseases (NCDs) is rapidly increasing worldwide. A general consensus at the 2011 United Nations high level meeting

on NCDs affirmed that they jointly became the leading causes of deaths globally, and are expected to account for about 52 million deaths by 2030 (1, 2). The focus of the World Health Organization (WHO) and many stakeholders has turned towards addressing this burden more actively, especially in Africa and other low- and middle-income countries (LMIC), where a large public health burden is still being caused by infectious diseases (2). Africa is currently experiencing the fastest rate of urban development worldwide (2, 4). With increasing standard of living and improved care seeking, life expectancy across many African nations will continue to rise (4). The growing burden of NCDs in Africa is partly due to demographic changes and ageing of the population, and partly to rapid urbanization and adoption of urban lifestyles (2, 5). In combination, these two main drivers of the pandemics of NCDs are likely to increase both the prevalence and the absolute number of cases for many NCDs across Africa in the near future (2).

Chronic respiratory diseases (CRDs) rank among the leading causes of morbidity and mortality among NCDs worldwide, accounting for 4.7% of global disability-adjusted life years (DALYs), of which chronic obstructive pulmonary disease (COPD) is responsible for about two-thirds (5). According to 2008 global burden of disease (GBD) estimates, over 600 million have allergic rhinitis, 300 million people have asthma, and 210 million people have COPD (1, 6, 7). The WHO also estimates that COPD is responsible for about 3 million deaths globally in 2011, accounting for about 9.1% of all NCDs deaths (8). COPD is currently the fourth leading cause of death globally and is projected to be the third leading cause of death by 2030 (8), by which point it is expected to overtake HIV/AIDS as the leading cause of death in Africa (9).

The increasing burden of COPD in Africa can be attributed to factors such as tobacco smoking, environmental pollution, exposure to combustion products of biomass fuels (from coal, firewood and agricultural residue), occupational dusts, tuberculosis, and long-term sequelae of childhood respiratory infections (10). Attempts at reducing this burden have been hindered mainly due to: inadequate standards of health promotion and other health services; insufficient attention from health planners, government regulators and media; absence of national guidelines on the management of COPD and lack of funds (11, 12). In fact, in many urban African settings, reports reveal an increasing consumption of tobacco products (10), which is made worse due to lack of government regulations on tobacco sales and use (10, 11). In some mixed, urban and rural settings, most households still use firewood and charcoal for domestic cooking and many countries are yet to implement control strategies for biomass fuel exposure (10, 12).

The treatment of COPD in many resource-poor settings has also been a huge challenge (13). Inhaled steroids, which are an effective treatment of COPD, have been included in the amended WHO list of essential medicines (10). However, these are mostly unavailable and/or unaffordable in many African settings (9, 14). In fact, policymakers in some African countries have stated that it may be unrealistic to assume that essential drugs for treating COPD and other CRDs can be given free to patients (11, 14). This raises critical questions of equity and priority setting, since drugs for HIV/AIDS and tuberculosis are typically supplied free in Africa (9, 11).

Moreover, there is a lack of standard treatment guidelines and protocols for the management of COPD, and when available, health workers have not been adequately trained to identify and treat the disease (15). Lung function assessment is vital to COPD diagnosis and in quantifying airflow obstruction, and this is often needed to differentiate COPD from other obstructive airway diseases (11). It has been reported that spirometer, peak flow meter, and simple lung function test apparatus are scarcely available in many African settings and most treatments have mainly been based on acute exacerbations rather than an overall disease management plan (11, 16). Therefore, delayed diagnosis of COPD typically follows lengthy periods of hesitation from doctors and concerns raised by patients and their families (10, 17).

The understanding of the epidemiology of COPD on the African continent is still very limited (11). Although systematic reviews have been conducted on COPD in Africa (10–12), only one of them is about the continent-wide burden of COPD, while two other two focused on sub-Saharan Africa. These reviews mainly provided a systematic presentation of the available evidence, but there is still a need to further analyse the available studies to understand the appropriateness of the case definition used (spirometry vs non-spirometry data) and the effects of covariates such as sex, age, year of the study and country of the study. Researchers, policy makers and other stakeholders in Africa could be assisted with such information in designing further studies. Therefore, in this paper we aim to provide a deeper insight in the problem of COPD in Africa, by examining and comparing the two available types of data (spirometry-based and other) and investigating the role of covariates on the prevalence of COPD in Africa.

Methods

Search strategy and data sources

After identifying the relevant Medical Subject Headings (MeSH) and keywords, a systematic search of Medline, EMBASE and Global Health was conducted. The publication period studied was from January 1990 up to September 2013. Further relevant studies were identified through searching the references of all selected studies. African countries were included based on the World Bank list of economies (July 2012) (22). The search terms employed are shown in Table 1. No language restrictions were applied.

Characteristic features of the identified African studies

Primary research on COPD in Africa has been very limited. This has in part been linked to challenges in

Table 1. Search terms

1	africa/ or exp africa, northern/ or exp algeria/ or exp egypt/ or exp libya/ or exp morocco/ or exp tunisia/ or exp "africa south of the sahara"/ or exp africa, central/ or exp cameroon/ or exp central african republic/ or exp chad/ or exp congo/ or exp "democratic republic of the congo"/ or exp equatorial guinea/ or exp gabon/ or exp africa, eastern/ or exp burundi/ or exp djibouti/ or exp eritrea/ or exp ethiopia/ or exp kenya/ or exp rwanda/ or exp somalia/ or exp sudan/ or exp tanzania/ or exp uganda/ or exp africa, southern/ or exp angola/ or exp botswana/ or exp lesotho/ or exp malawi/ or exp mozambique/ or exp namibia/ or exp south africa/ or exp swaziland/ or exp zambia/ or exp zimbabwe/ or exp africa, western/ or exp benin/ or exp burkina faso/ or exp cape verde/ or exp cote d'ivoire/ or exp gambia/ or exp ghana/ or exp guinea/ or exp guinea-bissau/ or exp liberia/ or exp mali/ or exp mauritania/ or exp niger/ or exp nigeria/ or exp senegal/ or exp sierra leone/ or exp togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp Emphysema/
13	copd.mp.
14	exp bronchitis, chronic/ or exp pulmonary disease, chronic obstructive/ or exp pulmonary emphysema/
15	12 or 13 or 14
16	1 and 11 and 15

Table 2. GOLD and ATS/ERS COPD diagnostic criteria

GOLD criteria (20)	
Stage	**Definition**
I	$FEV_1/FVC < 0.7$ $FEV_1 \geq 80\%$ predicted
II	$FEV_1/FVC < 0.7$ FEV_1 50–80% predicted
III	$FEV_1/FVC < 0.7$ FEV_1 30–50% predicted
IV	$FEV_1/FVC < 0.7$ $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure
ATS/ERS criteria (21)	
Severity	**Definition**
At risk Patients who: – Smoke/Pollutant exposure – Cough/Sputum/Dyspnoea – Family history of respiratory disease	Post-bronchodilator $FEV_1/FVC > 0.7$ $FEV_1 \geq 80\%$ predicted
Mild COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$ $FEV_1 \geq 80\%$ predicted
Moderate COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$ FEV_1 50–80% predicted
Severe COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$ FEV_1 30–50% predicted
Very Severe COPD	Post-bronchodilator $FEV_1/FVC \leq 0.7$ $FEV_1 < 30\%$ predicted

ATS: American Thoracic Society, ERS: European Respiratory Society, FEV_1: forced expiratory volume in one second, FVC: forced vital capacity, GOLD: Global Initiative for chronic Obstructive Lung Disease.

the accurate diagnosis of this condition and the heterogeneity of published research protocols (18). Various published reports have noted that symptoms of COPD, asthma and other obstructive airway diseases do overlap, which often complicates the case ascertainment in research studies (3). COPD has been previously described in terms of its clinical and pathological presentation, mainly as "chronic bronchitis" and "emphysema" (19). These, however, have not adequately explained the basic physiological impairment of the lungs in a COPD patient that, according to pulmonologists, can be traced to a reduced expiratory volume compared to the vital capacity of the lungs (10, 19). The Global Initiative on Obstructive Lung Disease (GOLD) and the 'American Thoracic Society/ European Respiratory Society' (ATS/ERS) have provided clear definitions of COPD based on spirometry (defined as a ratio of forced expiratory volume in one second to forced vital capacity less than 70% ($FEV_1/FVC < 0.7$) (20, 21), see Table 2.

Since the publication of GOLD and ATS/ERS criteria, research outputs from Africa have still remained low, with the few COPD studies from Africa being mainly non-spirometric studies (11). Furthermore, existing reviews have identified only ten countries in Africa that have conducted and published research findings on COPD and these are mainly from selected populations and occupational settings where the case definitions were mostly based on respiratory symptoms (10). These have all limited on-going research efforts towards determining the true burden of COPD in Africa.

Study selection

A parallel search and double extraction of data was conducted by the first two co-authors. We retained original population-based studies on COPD and/or chronic bronchitis conducted in urban, rural or occupational settings within African population groups. We also ensured that the retained studies provided numerical estimates on the prevalence of COPD and/or chronic bronchitis, and had clearly defined methodologies. We excluded studies that were hospital-based, had non-human subjects, have been conducted before 1990, or that were review publications.

Case definitions needed to comply with:

i) the Global Initiative on Obstructive Lung Disease (GOLD) criteria (20);
ii) the American Thoracic Society/ European Respiratory Society (ATS/ERS) criteria (21), {with GOLD and ATS/ERS criteria both broadly defined as a post-bronchodilatory (PBD) ratio of forced expiratory volume in one second to forced vital capacity of less than 70% (PBD $FEV_1/FVC < 0.7$)}; and/or

iii) the 1965 British Medical Research Council (BMRC) definition of chronic bronchitis, defined as "chronic productive cough on most days for 3 months in 2 consecutive years in a person in whom other causes of chronic productive cough have been excluded" (20, 21), see Table 1 for detailed diagnostic criteria.

Data extraction and analysis

Data have been extracted from the retained studies and included information concerning the corresponding country, the study period, the mean age (and any age groups that were studied specifically), the number of cases, the sample size and the prevalence of COPD. Studies were broadly grouped into "spirometric" (defined as complying with case definitions 'i and ii', as mentioned above) and "non-spirometric" (defined as complying with case definitions 'iii'). For studies conducted on the same study site, population or cohort, the first chronologically published study has been considered, with all additional new data from more recent studies further added.

For our analysis, the prevalence of COPD was separately investigated from "spirometric" and "non-spirometric" sets of studies and the effect of covariates (e.g., mean age, gender, year of study and the country). In addition, the prevalence of COPD from the two types of studies was compared. We used Pearson correlation coefficients, *t*-test on equality of means, and the Mann-Whitney test for equality of medians to study the effects of case definition and other covariates on the prevalence of COPD. We used the median and inter-quartile range from spirometry-based studies and the United Nation Population Division's population figures to estimate the number of COPD cases in the year 2010.

Results

Systematic review

Our search has returned 243 studies: Medline (66), EMBASE (144), and Global Health (33). After screening the titles for relevance and excluding duplicates, 134 publications were selected. Sixty-nine abstracts satisfied our inclusion criteria. After applying the quality criteria, i.e. studies with clear case definitions and sampling methods, 58 studies were excluded. Two additional studies have been included from the search of the reference lists of the selected studies. A total of 13 studies met the quality criteria and thus have been included in our study (Figure 1).

Study characteristics

From the retained studies (23–35), 7 were conducted in South Africa and Nigeria. Other countries represented were Algeria, Ethiopia, Malawi, Morocco, Rwanda and Tunisia. There were 5 spirometric (23, 27–29, 31) and 10 non-spirometric studies (24–26, 28, 30–35), with 13 and 20 data points, respectively; two studies reported both spirometric and non-spirometric estimates (28, 31)

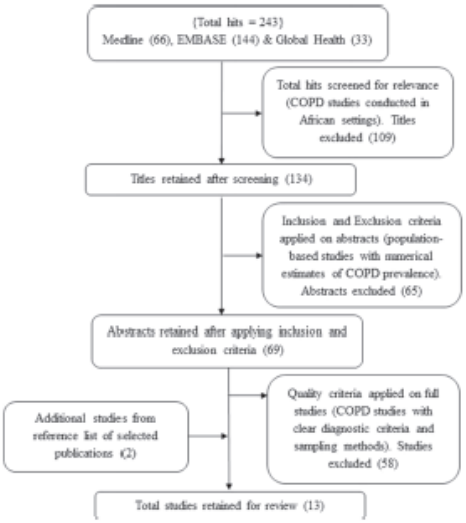

Figure 1. Flow chart of the study selection.

(Tables 3 and 4). All studies focussed on subjects with a mean age of 55.2 years and 49.2 years in spirometric and non-spirometric studies, respectively. Across many studies, birth certificates were usually employed in determining the age of subjects, and in the absence of valid age-verification documents, historical landmarks were employed. Studies were conducted mostly within one year (7 studies), overall mean sample size was 1241 (median 416), and study settings were predominantly mixed (urban and rural) (6 studies).

Prevalence estimates

First, we report separately the estimates of the prevalence of COPD for the two types of data: spirometry-based and all other studies (Table 5; Figure 2). The median prevalence of COPD from spirometry-based studies is 13.4% (IQR: 9.4%–22.1%), while for all other studies it is 4.0% (IQR: 2.1%–8.9%). This difference is statistically significant ($p = 0.001$ for comparison of medians and $p = 0.003$ for comparison of means). The descriptive statistics for other covariates, such as the year of study, mean age, the number of cases and sample size are shown in Table 5.

A significant positive correlation has been demonstrated between the prevalence of COPD and the mean age in the spirometry-based set of studies (see Figure 3), with the Pearson correlation coefficient of 0.645 (p-value = 0.017). This is a plausible finding that suggests internal consistency of spirometry-based estimates, while this trend was not observed in studies using other case definitions. Moreover, no significant correlation could be demonstrated between the prevalence of COPD and the

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Table 3. Overall study characteristics

Author	Country, Location	Study setting	Study period	Age range/Mean age	Case definition
Ayo-Yusuf et al. (33)	South Africa, National DHS	Mixed	1998	≥25 years	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Buist, A.S. et al. (23)	South Africa, Cape town	Mixed	2004–2006	≥40 years	GOLD criteria: postbronchodilator $FEV_1/FVC < 0.7$
Desalu OO (24)	Nigeria, Ekiti State	Rural	2009	≥35 years (mean age 55.5 ± 10.2)	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Desalu et al. (25)	Nigeria, Ijero-Ekiti	Rural	2009	55 ± 10 years	ECRHS & BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Ehrlich, R.I. et al. (26)	South Africa, National Household Survey	Mixed	2004	≥15 years	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Fullerton, D.J. et al. (27)	Malawi, Blantyre and Chikwawa districts	Mixed Urban and Rural	2001	≥30 years (mean age 45.0 years)	ATS/ERS criteria: $FEV_1/FVC < 0.7$
Gathuru, I.M. et al. (28)	Nigeria, Benin	Urban	1992–1999	30–69 yrs (mean age 48.8 years)	ATS/ERS criteria: $FEV_1/FVC < 0.7$; BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Girdler-Brown et al. (31)	South Africa, Basotho	Occupational	2007–2008	Mean age 49.4 years	ATS/ERS criteria: $FEV_1/FVC < 0.7$; BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Khelafi, R. et al. (29)	Algeria, Algiers	Mixed	2009	21–89 years	GOLD criteria: postbronchodilator FEV1/FVC < 0.7
Laraqui Hosni et al. (32)	Morocco, Rabat	Occupational	2001–2002	≥15 years	BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Mengesha & Bekele (34)	Ethiopia, Addis Ababa	Occupational	1997–1998	37 ± 8.0 years	BMRC (1965) & ATS (1962) criteria: productive cough for >3 months/year for at least 2 successive years
Musafiri, S. et al. (30)	Rwanda, Kigali	Mixed	2008–2009	≥15 years (mean age 38.3 years)	ATS/ERS guidelines: $FEV_1/FVC <$ LLN. LLN = lower limit of normal, which is 5th percentile (1.645 SD below predicted); BMRC criteria: cough with phlegm every day for at least 3 months a year for at least 2 successive years
Tabka et al. (35)	Tunisia, Tunis	Occupational	1998	≥15 years	BMRC criteria: productive cough for >3 months/year for at least 2 successive years

ATS: American Thoracic Society, BMRC: British Medical Research Council, DHS: Demographic and Health Survey, ECRHS: European Community Respiratory Health Survey, ERS: European Respiratory Society, FEV1: Forced Expiratory Volume in 1 second, FVC: Forced Vital Capacity, GOLD: Global Initiative for chronic Obstructive Lung Disease, LLN: lower limit of normal.

year of study or gender for both data sets (see Supplementary Online Material).

When applied to the appropriate age group (40 years or more), which accounted for 196.4 million people in Africa in 2010, the estimated prevalence translates into 26.3 million (18.5–43.4 million) cases of COPD. Comparable figures for the year 2000 based on the same prevalence rates would amount to 20.0 million (14.1–33.1), suggesting an increase of 31.5% over a decade that is attributable to ageing of the African population alone.

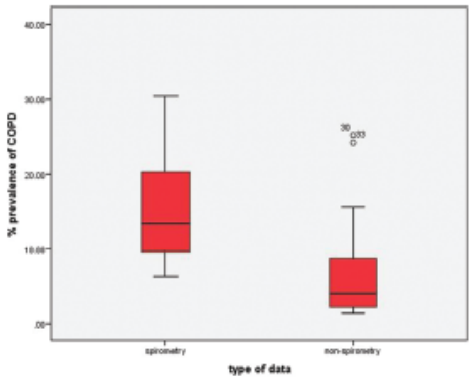

Figure 2. Boxplots of the prevalence of COPD for the studies based on spirometry and all other studies.

Discussion

Although we recognize that there may be on-going efforts to estimate the prevalence of COPD in Africa by other research groups, among which the BOLD initiative is particularly prominent (36), this study—to the best of our knowledge—provides the first systematic continent-wide estimates of COPD prevalence in Africa. Our results show a significant association between patient's age and COPD prevalence in a spirometry-based data set (4, 37–39), and further point out the statistically significant differences between spirometry and non-spirometry data, among which spirometry-based estimates generally appear more homogenous and internally consistent.

The 2006 BOLD study (conducted across 12 sites globally) reported a global COPD prevalence of 10.1%

Table 4. Distribution of studies

Country	Number of studies
Algeria (29)	1
Ethiopia (34)	1
Malawi (27)	1
Morocco (32)	1
Nigeria (24, 25, 28)	3
Rwanda (30)	1
South Africa (23, 26, 31, 33)	4
Tunisia (35)	1
Study type	
Spirometric (23, 27–29, 31)	5
Non-spirometric (24–26, 28, 30–35)	10
Studies reporting both (28, 31)	2
Study setting	
Rural (24, 25)	2
Urban (28)	1
Mixed (23, 26, 27, 29, 30, 33)	6
Occupational (31, 32, 34, 35)	4
Study duration	
<1 year (24–27, 29, 33, 35)	7
1–3 years (23, 30–32, 34)	5
>3 years (28)	2
Sample size	
<1000 (23–25, 27, 28, 31, 32, 34, 35)	9
1001–3000 (29, 30)	2
>3000 (26, 33)	2

(male 11.8%; female 8.5%) using GOLD criteria (23). They did not quote overall estimates for Africa, as South Africa was the only African study site (23). However, that study reported a COPD prevalence of 22.2% and 16.7% in South Africa among men and women aged ≥40 years, respectively, which seems very high and it's unlikely to be representative for the rest of Africa (23). In other studies, conducted among community-based population samples, a spirometric prevalence of 13.6% was estimated in Malawi and 9.2% in Algeria (27, 29). Other studies conducted in Africa were mainly non-spirometric with low recorded prevalences (Nigeria 5.6%, South Africa 2.6% and Algeria 1.7%) (24, 26, 29). These are the major population-based studies on COPD conducted in Africa, with no systematic continent-wide prevalence estimates published.

Our mean and median prevalences from all study populations were higher for the spirometric studies compared to non-spirometric studies (Table 5), which supports previous reports on the under-estimation of COPD from non-spirometric studies (23).

Based on the retained studies, we note that the prevalence of smoking was high in some study populations, with odds of having COPD among current smokers estimated at 6.37 (Nigeria), 3.22 (Rwanda), and 1.15 and 2.84 (South Africa) (23, 24, 30, 33) (Table 6). It is important to note that this study is not a comprehensive review of smoking prevalence in Africa, as there were only four studies reporting COPD risks among current smokers (23, 24, 30, 33); it may therefore be inappropriate to draw conclusions based on this. However, some authors warned that Africa is on the verge of a smoking

Table 5. Statistics for year, mean age, number of cases, sample size and prevalence of COPD for the spirometry-based studies and all other studies

Spirometry-based studies						
Statistics		Year	Mean age	No. of cases	Sample size	% prevalence of COPD
Data points		13	13	13	13	13
Mean		2004.85	55.2462	55.57	389.85	15.5946
Median		2006.00	53.5000	45.00	290.00	13.4000
Std. Deviation		3.934	11.49461	50.329	285.518	7.91887
Range		10	39.50	191	896	24.15
Percentiles	25	2000.00	46.9000	20.11	160.00	9.3700
	75	2008.50	62.0000	77.84	633.00	22.0500
Other studies						
Statistics		Year	Mean age	No. of cases	Sample size	% prevalence of COPD
Data points		20	20	20	20	20
Mean		2004.65	49.1750	68.52	1797.10	7.0015
Median		2004.00	49.1000	55.50	516.00	4.0350
Std. Deviation		4.043	14.29497	84.273	3044.636	7.18240
Range		11	60.00	358	13411	23.80
Percentiles	25	2002.50	39.5000	6.81	116.75	2.1225
	75	2009.00	58.5000	80.00	2260.50	8.8500

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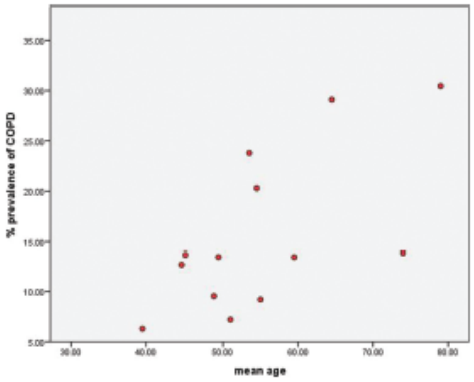

Figure 3. Plot of the prevalence of COPD versus the mean age from the spirometry-based studies.

epidemic due to a rapidly spreading tobacco market in the continent, and could be contributing to the growing burden of chronic respiratory diseases in the region (43).

For example, Jha and colleagues reported an increasing prevalence of smoking in Africa with an overall prevalence of 18% in 1995 (44). In addition, a systematic review of studies conducted among persons aged 15 years or more, across 14 countries in sub-Saharan Africa (SSA), reported smoking prevalence ranging from 6% to 24% between 1996 and 2005, with a high proportion of young smokers (45). The increasing prevalence was further underpinned in a 2006 demographic health survey, also conducted across 14 countries in SSA, with reported smoking prevalence ranging from 8% to 27% (46). Moreover, some other research findings have shown that COPD prevalence in many parts of the world increases along with the increasing number of cigarette packs per year, with findings in some African population groups suggesting they could be more prone to the health risks from tobacco smoke than people living in other world regions (10, 23, 47).

Meanwhile, according to the 2010 Institute for Health Metrics and Evaluation (IHME) global burden of disease studies, the DALYs and deaths for COPD decreased between 1990 and 2010 by 2.0% and 6.4% respectively (DALYs decreased from 78.3 to 76.7 million, and deaths from 3.1 to 2.9 million) (5, 48). These are global estimates based on complex modelling, and we appreciate that these may not necessarily reflect the COPD prevalence in Africa for many different reasons, including (but not limited to) contextual, socio-economic, demographic and ethnic differences in many regions of the world. Furthermore, many concerns have been raised about the choice of data and modelling methods used in the GBD 2010, so we should treat their estimates with caution until they are independently confirmed (49, 50).

Although we aimed to provide an evidence-based and data driven prevalence estimate of COPD in Africa, the current low research output and the major gaps in data availability from many countries have greatly limited our analysis. We thus understand there could be uncertainties surrounding the estimates of the prevalence of COPD, such as variations in population structures, diagnoses, sampling methods, and effects of other health determinants (beyond the age of patients). First, the number of retained studies was very low, with only 8 African countries represented, and over 50% of datapoints originating from South Africa and Nigeria. Our results may therefore tend to reflect more the COPD burden in these two countries and limit their generalizability to other African countries, given that those are relatively wealthy countries in African terms. Second, the overall sample size was relatively small (at 24,747), with a mean and median sample size per study of 1,767 and 416, respectively. Third, there were significant variations in diagnostic criteria and survey methodologies across studies. Most retained studies were population-based cross-sectional studies. However, due to the very limited evidence base and due to the published reports that occupational COPD contributes significantly to the global burden of chronic respiratory diseases (51), we also included studies conducted in occupational settings. As this is strictly within a population where subjects have been exposed over time to COPD risks, we understand this may potentially increase our prevalence estimates. Finally, we mention that across all studies, data on age- and sex-specific prevalence, including corresponding data on urban-rural settings were not always provided, although they are of vital importance to perform further comparisons and reach conclusions

Table 6. Prevalence of COPD in terms of smoking from selected studies

Author	Study setting	Sample size	COPD prevalence (%)	Current smokers (%)	Odds ratio of COPD among current smokers (95% CI)
Ayo-Yusuf et al. (33)	Mixed	4464	3.2	7.3	2.84 (1.60, 5.04)†
Buist, A.S. et al. (23)	Mixed	847	23.8	30.0*	1.15 (1.00, 1.32)**
Desalu OO (24)	Rural	391	5.6	2.6	6.37 (2.12, 19.4)
Ehrlich, R.I. et al. (26)	Mixed	13468	2.6	21.7	–
Gathuru, I.M. et al. (28)	Urban	270	9.5	10.8	–
Musafiri, S. et al. (30)	Mixed	1824	4.5	16.7	3.22 (1.53, 4.31)

†odds ratio in women, *20 pack-years, **10 pack-years.

about the prevalence of COPD in specific age groups or settings.

Public health response to COPD in Africa

A major setback in the fight against the growing burden of COPD in Africa is the relative neglect by the governments of many African nations. COPD is thought to be a rather complex disease, usually self-inflicted, irreversible, and difficult to treat (52, 53). Many African governments have not set up awareness campaigns and preventive programmes that can help address these issues (9). There is also the problem of unchecked urbanization, with no policies and or legislation to protect citizens from adverse effects, such as increase tobacco sales and use, and air pollution from industrial effluents, smoke and smog (10). For example, a study showed that less than 10% of the global population, especially in Africa, is fully protected by any form of tobacco-demand reduction measures (52). Addressing this is even more difficult because tobacco companies, which can be important drivers of some African economies, are using several tactics to resist regulation against its products, including: stressing the importance of tobacco to the economy of the countries that grow it, funding political parties, lobbying and influencing policies on tobacco products, preventing anti-smoking adverts and campaigns and buying off researchers and experts to create controversies on established facts on smoking (54, 55).

Furthermore, research findings have also shown that the risk of developing COPD from exposure to biomass fuels is comparable to the risk from tobacco smoking (6, 56). This is particularly significant in Africa, as about 90% of rural settings still rely on unprocessed biomass fuel for domestic cooking and heating, a situation made worse due to inadequate health awareness and intervention programmes reaching these settings (25). In fact, evidence is now emerging that due to erratic power supply and high costs of cooking gas in many African nations, the use of charcoal and firewood is gradually increasing among many urban dwellers, as this is now considered a cheap alternative for domestic cooking (3, 10). It is believed that an improved biomass stove and cooking environment remain the most cost-effective intervention for reducing the prevalence of COPD in sub-Saharan Africa (10).

Experts have reported that health sector reform programmes targeted at COPD and other chronic diseases in many African countries have not been very effective (16, 17). The Global Alliance against chronic Respiratory Diseases (GARD), an initiative of the WHO, recommends that a framework for chronic respiratory diseases surveillance should involve monitoring the exposures, outcomes and health system capacity response, and technically supporting appropriate interventions where and when necessary (57). According to WHO African Regional Office, GARD functions in Africa, but insufficient government support at a country level often leads to non-implementation of programmes (10). In addition, while appreciable health reforms and intervention programmes have been conducted in parts of Africa, adherence to these programmes at a community and individual level is low (3). For example, biomass stove intervention programmes in some areas have not been effective; reports show there are a wide range of national, regional, community and individual reasons why people may not adhere to the intervention programmes (9, 13). This further underscores the importance of understanding cultural backgrounds and social systems in an African setting towards improving acceptability of many interventions (10).

The delayed health care seeking behaviour in many African populations has also affected the management of COPD (10). For example, in a study of 298 patients attending respiratory clinics in rural South Africa, the observed median total delay to health facility was about 10 weeks, despite many being at severe stages of disease (58). This has been linked to high cost of health care, illiteracy and inherent cultural beliefs, with all these resulting in increased patronage of traditional (herbal) healers (9). Patients often present back at health centres with complications from improper management given by the traditional healers (59).

In health service delivery, studies have reported that many health workers are ill-equipped in diagnosing COPD, making the under-diagnosis of COPD a problem confronting many African nations (40). Moreover, it is believed that the under-recognition of COPD in African countries may be because patients present late and, even after presentation to health services, diagnoses are typically delayed until the disease is relatively advanced (40, 41). Research findings have shown that lack of (use of) spirometers poses a very important practical challenge in rural settings with the main reasons being due to unavailability, improper usage, and low awareness of their importance (11). The unavailability and unaffordability of drugs have also affected health service delivery (10). Many countries provide free tuberculosis and HIV treatments, while essential drugs for COPD and other CRDs, such as inhaled beclomethasone, are either unavailable or unaffordable (6, 60). This unavailability of drugs may reflect lack of funds but may also be partly due to available limited funds being used inappropriately for expensive drugs that have no proven value in the management of COPD (10).

The relatively low income status in Africa is also contributory to the overall burden of COPD in Africa, especially at the family and individual levels. According to clinicians, poor living conditions, such as overcrowded homes, poor domestic cooking environment, and poorly ventilated houses, may worsen COPD; and due to the low income status, patients may still lack the financial resources to seek proper treatment (61, 62). Personal healthcare expenses in Africa are mostly out-of-pocket; there are no standard health insurance schemes as found in high-income settings (13).

The low level of published research on COPD and other CRDs has posed a major challenge to policymakers and many stakeholders, as there are not yet enough evidenced-based findings that can contribute to informed policy making to tackle this disease burden (59). The limited amount of published research in Africa may be due to challenges in conducting studies that would fully adhere to internationally agreed case definitions (40). For example, many studies now use post-bronchodilatory spirometry as a gold standard (42); whereas others state that using post-brochodilator estimates may result in a 5–50% reduction in prevalence compared to pre-bronchodilator values (39). It has been suggested that the low research output reflects the poor recent availability of research funding for COPD by funding agencies, which in turn reflects their lack of priority given to COPD (11, 16). The research priorities of many African governments still focus on communicable diseases, notably HIV/AIDS, tuberculosis and malaria (63, 64). In addition, the influence of the tobacco industry, which financially supports many governments in Africa, may also have negatively affected research output in the field (10, 65, 66).

Conclusion

The data on COPD in Africa is limited, with the few published studies only available from some countries in Africa. However, it is evident from those studies that the burden of COPD in Africa is significant. With continued urbanization, rapid ageing and lack of corresponding measures to check the effects on the population, the burden of COPD will continue to grow and it is set to become one of the major public health problems in Africa.

There is need for more research on COPD prevalence, incidence, sequelae and mortality, along with well-designed trials, to identify how to effectively reduce risks from exposure to biomass fuels and tobacco smoking. With improved awareness of this problem, policy makers and governments of many African nations should give more attention to NCDs such as COPD, fund relevant research to improve evidence for decision making, and thus make informed decisions on preventive and treatment strategy options, and so help counter the rising disease burden over the next decade.

Declaration of Interests Statement

All co-authors designed and conducted the study and contributed to the writing of the paper.

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author). The authors declare no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; and no other relationships or activities that could appear to have influenced the submitted work; apart from that declared under "funding."

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An estimate of asthma prevalence in Africa: a systematic analysis

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Aim To estimate and compare asthma prevalence in Africa in 1990, 2000, and 2010 in order to provide information that will help inform the planning of the public health response to the disease.

Methods We conducted a systematic search of Medline, EMBASE, and Global Health for studies on asthma published between 1990 and 2012. We included cross-sectional population based studies providing numerical estimates on the prevalence of asthma. We calculated weighted mean prevalence and applied an epidemiological model linking age with the prevalence of asthma. The UN population figures for Africa for 1990, 2000, and 2010 were used to estimate the cases of asthma, each for the respective year.

Results Our search returned 790 studies. We retained 45 studies that met our selection criteria. In Africa in 1990, we estimated 34.1 million asthma cases (12.1%; 95% confidence interval [CI] 7.2-16.9) among children <15 years, 64.9 million (11.8%; 95% CI 7.9-15.8) among people aged <45 years, and 74.4 million (11.7%; 95% CI 8.2-15.3) in the total population. In 2000, we estimated 41.3 million cases (12.9%; 95% CI 8.7-17.0) among children <15 years, 82.4 million (12.5%; 95% CI 5.9-19.1) among people aged <45 years, and 94.8 million (12.0%; 95% CI 5.0-18.8) in the total population. This increased to 49.7 million (13.9%; 95% CI 9.6-18.3) among children <15 years, 102.9 million (13.8%; 95% CI 6.2-21.4) among people aged <45 years, and 119.3 million (12.8%; 95% CI 8.2-17.1) in the total population in 2010. There were no significant differences between asthma prevalence in studies which ascertained cases by written and video questionnaires. Crude prevalences of asthma were, however, consistently higher among urban than rural dwellers.

Conclusion Our findings suggest an increasing prevalence of asthma in Africa over the past two decades. Due to the paucity of data, we believe that the true prevalence of asthma may still be under-estimated. There is a need for national governments in Africa to consider the implications of this increasing disease burden and to investigate the relative importance of underlying risk factors such as rising urbanization and population aging in their policy and health planning responses to this challenge.

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Chronic respiratory diseases (CRDs) are among the leading causes of death worldwide, with asthma rated the most common chronic disease affecting children (1). Globally, about 300 million people have asthma, and current trends suggest that an additional 100 million people may be living with asthma by 2025 (1,2). The World Health Organization (WHO) estimates about 250 000 deaths from asthma every year, mainly in low- and middle-income countries (LMIC) (3,4). Just like with many other chronic diseases in Africa, the fast rate of urbanization has been linked to the increase in the burden of asthma and other allergic diseases (3,5,6). The prevalence of these conditions may, in theory, have the potential to reach levels higher than those observed in high-income countries (HIC) due to priming effects of parasitic helminthic infections on the immune system, as these infections are common in many African settings (5). The International Study of Asthma and Allergies (ISAAC) reported that asthma prevalence among children was increasing in Africa and has contributed most to the burden of disease through its effects on quality of life (3). In-patient admissions and purchase of medications account for most of the direct costs on government, while loss of productivity, due to absenteeism from work and school, are responsible for most of the indirect costs (7,8).

Asthma is widely known as a multifactorial respiratory disorder with both genetic and environmental underlying risk factors (3). Exposure to common allergens (including pollens, dust mites, and animal furs) and indoor and outdoor air pollution from various sources (eg, traffic pollution, combustion of fossils and biomass fuels, workplace dust) have all been implicated as triggers of the disease (9). Second hand tobacco smoking is a confirmed risk factor in pediatric patients (5,10). Viral infections, a major cause of upper respiratory tract infections and "common cold," are also a common risk factor in children (11,12). As noted, helminthic infections are relatively common in Africa and are associated with bronchial hyper-responsiveness and asthma (5,13); this is perhaps due to the presence of related raised immunoglobulin E (IgE) and a prominent Th2 immune response (5,14).

Studies on asthma are few in Africa, with most publications mainly from South African and Nigerian populations (14). One main factor affecting research output is the diagnosis of asthma, which still remains a challenging issue (15,16). The WHO has emphasized that this has limited on-going research efforts globally (4,16). The International Union against Tuberculosis and Lung Diseases (IUATLD) published one of the first diagnostic and survey guidelines for asthma in 1984, but experts subsequently reported concerns about its precision and reliability (17). According to the Global Initiative for Asthma (GINA), detailed history, physical examination and spirometric lung function tests are vital to the diagnosis and management of asthma (10,18). Generally, a reduction in forced expiratory volume in one second (FEV_1) and peak expiratory flow (PEF) may be indicative of asthma, with the amount of reduction proportional to the severity of asthma (4). GINA proposed that an increase in FEV_1 of >12% and 200 mL in about 15-20 minutes following the inhalation of 200-400 µg of salbutamol or a 20% increase in PEF from baseline can be employed as standardized criteria in diagnosis of asthma (10). This, however, lacks sensitivity, as many asthmatics, especially those on treatment, may not exhibit an increase in FEV_1 and PEF when assessed (16,19). Thus, although asthma is characterized by significant reversibility of airway obstruction, an absence of reversibility may not always exclude the presence of asthma (20). The ISAAC established in 1991, remains the largest epidemiological study among children globally (1). ISAAC methodologies and scoring are currently the most widely employed by researchers in Africa (1,4). This involves both video and written questionnaires, as there were reports that video and pictorial representations of asthma symptoms may contribute to improved case recognition in younger children (1). However, this is still a subject of debate among experts (21). The European Community Respiratory Health Survey (ECRHS), which assessed the prevalence of atopy and symptoms of airway disease among older age groups in Western Europe, has been widely implemented and has reported significant geographic variations in the prevalence of asthma and atopy (9). Despite these revised guidelines, both ISAAC and ECRHS research groups have reported challenges in achieving high sensitivity and specificity in case ascertainment with the symptom "wheeze at rest in the last 12 months" (also regarded as current wheeze, or active wheeze), yielding the highest sensitivity and specificity (1).

In Africa, problems including those arising from the over-utilization of health services, lack of trained staff and diagnostic apparatus, and non-availability and unaffordability of inhaled medications have hindered efforts to improve the management of asthma (22,23). The lack of organized health promotion programs, such as effective control strategies for environmental triggers, air pollutants, and occupational dusts have also contributed to the growing burden (24). The WHO has reported that the levels of asthma control and health responses in the continent have been

below recommended standards, and that these have contributed to the size of the disease burden (3,4). In addition, although many African countries have national guidelines for the management of asthma and other CRDs, these guidelines have not been implemented in most rural areas (25,26). Economic analyses in many African settings have shown that direct costs from asthma are usually greater than the indirect costs. However, indirect costs represent a relatively higher proportion of total costs among pediatric than adult patients (8). Moreover, the wider economic burden on individuals, families, employers, and society, due to loss of future potential source of livelihood, has also been devastating in many resource-poor settings (22). It is believed that many children with asthma in Africa may fail to achieve their full potential if proper management and control measures are not put in place (1). It has been suggested that education of health care providers and the public is a vital element of the response to the challenge posed by asthma in Africa (4,27).

By 2015, it is expected that world's urban population will increase from 45% to 59%, with over half of this occurring in Africa (8). It is also expected that the prevalence of asthma and many chronic diseases in Africa will increase due to this growing population size and from effects of accompanying urbanization and adoption of western lifestyles (28). In light of this and of the low research output and poor availability of health services data on the burden of asthma in Africa, it is important to analyze the available data through a systematic review of the literature in order to attempt to quantify the burden, guide health priority settings, and inform the formulation of an appropriate health policy response.

METHODS

Search strategy and selection criteria

We conducted a systematic search of Medline, EMBASE, and Global Health. After an initial scoping exercise to identify Medical Subject Headings (MESH) and keywords, we developed a final search strategy. We further handsearched reference lists of retained publications for more relevant studies. African countries were included as contained in the World Bank list of economies from July 2012 (29) (Table 1).

We retained cross-sectional population-based studies on asthma conducted primarily on African population groups. The date of publication was set from 1990 to June 2013. We included studies providing numerical estimates on the prevalence of asthma, including non-English publications. We excluded studies that were mainly reviews, hospital-based (without a denominator population estimate), without numerical estimates, and conducted on non-human subjects.

Studies were further checked for clear diagnostic criteria and survey methods. As noted above, asthma has been described in various ways by many researchers, we therefore allowed for these variations in our analysis (Table 2 and Supplementary Table 1). However, most survey methods were mainly based on written or video questionnaires, as proposed by the ISAAC study group (Table 3 and Supplementary Table 1).

Data extraction and analysis

Relevant data were extracted from retained studies and saved in Microsoft Excel file-format. All data were double

TABLE 1. Search terms used in the study

1	africa/ or exp africa, northern/ or exp algeria/ or exp egypt/ or exp libya/ or exp morocco/ or exp tunisia/ or exp "africa south of the sahara"/ or exp africa, central/ or exp cameroon/ or exp central african republic/ or exp chad/ or exp congo/ or exp "democratic republic of the congo"/ or exp equatorial guinea/ or exp gabon/ or exp africa, eastern/ or exp burundi/ or exp djibouti/ or exp eritrea/ or exp ethiopia/ or exp kenya/ or exp rwanda/ or exp somalia/ or exp sudan/ or exp tanzania/ or exp uganda/ or exp africa, southern/ or exp angola/ or exp botswana/ or exp lesotho/ or exp malawi/ or exp mozambique/ or exp namibia/ or exp south africa/ or exp swaziland/ or exp zambia/ or exp zimbabwe/ or exp africa, western/ or exp benin/ or exp burkina faso/ or exp cape verde/ or exp cote d'ivoire/ or exp gambia/ or exp ghana/ or exp guinea/ or exp guinea-bissau/ or exp liberia/ or exp mali/ or exp mauritania/ or exp niger/ or exp nigeria/ or exp senegal/ or exp sierra leone/ or exp togo/
2	exp vital statistics/ or exp incidence/
3	(incidence* or prevalence* or morbidity or mortality).tw.
4	(disease adj3 burden).tw.
5	exp "cost of illness"/
6	exp quality-adjusted life years/
7	QALY.tw.
8	Disability adjusted life years.mp.
9	(initial adj2 burden).tw.
10	exp risk factors/
11	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12	exp asthma/ or exp asthma, aspirin-induced/ or exp asthma, exercise-induced/ or exp asthma, occupational/ or exp status asthmaticus/
13	1 and 11 and 12

extracted and sorted by country, study period, age, and their respective case number, sample size, and prevalence estimate. Extracts were grouped into data from written questionnaires or video questionnaires, both including data based on asthma diagnosis, and/or its symptoms (wheeze at rest, wheeze on exercise, nocturnal wheeze, nocturnal cough, or severe wheeze). For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, with all additional data from other studies added to that of the selected paper.

For our analysis, weighted means of asthma symptoms were calculated (pooled from reported crude prevalences in individual studies) and expressed in percentages. Asthma prevalence estimates based on "current wheeze" (wheeze at rest- 12 months) have high sensitivities and specificities (1,17, 30); we therefore applied extracted values from this in our modeling. Mean age and prevalence were plotted on bubble graphs, and the fitted curve explaining the largest proportion of variance (best fit) was applied. The equation generated determined the prevalence of asthma in Africa at midpoints of the United Nation population 5-year age-groups (for Africa) for the years 1990, 2000, and 2010.

RESULTS

Systematic review

Our main search returned 790 studies; Medline (n=246), EMBASE (n=370), and Global Health (n=174). After screening the titles for relevance (ie, asthma studies conducted primarily in an African population setting) and excluding duplicates, 147 studies were retained. 85 abstracts satisfied our selection criteria (ie, population-based studies providing numerical prevalence estimates of asthma). Applying the quality criteria (ie, studies with clear diagnostic criteria and survey methods), 43 studies were excluded. On hand searching reference lists of selected studies, further 3 studies were included, giving a total of 45 studies retained for the review (Figure 1).

Study characteristics

The 45 retained studies (12,20,31-73) covered most parts of Africa. South Africa (11 studies) and Nigeria (8 studies) had the highest publication outputs. Ethiopia and Kenya closely followed with 6 and 5 studies respectively, while Algeria, Morocco, and Tunisia in North Africa had 4 studies each. 14 studies were based on ISAAC guidelines and 31 non-ISAAC

TABLE 2. Asthma terms and definitions

Terms	Definition
Wheeze	A high pitched whistling sound originating from obstructed airways (1). "Wheeze at rest-12 months" refers to the prevalence of wheeze in a person in the last 12 mo.
Asthma	A chronic airway disease characterized by wheezing (a high pitched whistling sound originating from obstructed airways). Patient usually presents with chronic airways inflammation, bronchial hyper-responsiveness and reversible airflow obstruction, resulting in the recurrent attacks of wheeze, chest tightness, breathlessness, and occasionally cough and sputum production, all of varying severity and frequency from person to person (1,3,24,87). Asthma ever refers to cummulative prevalence of asthma in a person.
Asthma exacerbation	Also known as acute asthma. A sudden progressive episodes of shortness of breath, usually characterized by chest tightness, wheezing, cough, or sputum production (87)
Moderate asthma exacerbation	An event that, when recognized, should result in a temporary change in treatment, in an effort to prevent the exacerbation from being severe (24)
Severe asthma exacerbation	Events that require urgent action on the part of the patient and physician to prevent a serious outcome, such as hospitalization or death (24)
Severe asthma	Uncontrolled asthma which can result in risk of frequent severe exacerbations (or death), and/or adverse reactions to medications, and/or chronic morbidity, including impaired lung function or reduced lung growth in children (24)
Asthma control	Extent to which the various manifestation of asthma are reduced or removed by treatment (3,24)
Asthma diagnosis	GINA proposed a holistic approach involving detailed history, physical examination and spirometry. An increase in FEV1 of ≥12% and ≥200ml after a bronchodilator is indicative of reversible airflow limitation, which is consistent with asthma. Peak expiratory flow (PEF) with an improvement of 60l/min (or ≥20% of the pre-bronchodilator PEF) after a bronchodilator, or a diurnal variation in PEF of more than 20% (with twice daily readings more than 10%) may also be indicative of asthma. Other non-specific diagnostic tests include methacholine or histamine test, inhaled mannitol or exercise challenge, skin prick test and measurement of serum IgE (10,18)

*Abbreviations: FEV1 – forced expiratory volume in one second; GINA – Global Initiative for Asthma; IgE – immunoglobulin E; PEF – peak expiratory flow.

guidelines, while 39 studies employed written questionnaires and 6 used video questionnaires (Table 3).

Most studies were conducted mainly on pediatric subjects, mostly defined as less than 15 years of age. For the age determination of subjects from most studies, birth certificates were usually employed, and in the absence of valid age-verification documents, historical landmarks were employed.

TABLE 3. **Asthma study distribution**

Country:	Number of studies
Algeria (32,36,37,44)	4
Burkina Faso (55,56)	2
Cameroon (31)	1
Cape Verde (72)	1
Congo Brazzaville (31)	1
Cote d'Ivoire (31,47,63)	3
DR Congo (31,61)	2
Egypt (52)	1
Ethiopia (12,31,32,53,71,73)	6
Gabon (31)	1
Gambia (69)	1
Ghana (41)	1
Guinea (31)	1
Kenya (31,39,40,59,68)	5
Madagascar (66)	1
Morocco (32,34,44,48)	4
Mozambique (49)	1
Nigeria (31-33,38,45,50,51,58)	8
Rwanda (57)	1
South Africa (20,31,32,42,43,54,60,62,65,67,70)	11
Sudan (31,32)	2
Tanzania (35)	1
Togo (31)	1
Tunisia (32,44,46,64)	4
Duration of study:	
<1 y	23
1-3 y	16
>3 y	6
Sample size:	
<1000	18
1001-3000	15
>3000	12
Study setting:	
rural	3
urban	6
mixed	30
occupational	8
Study type:	
based on ISAAC guidelines*	14
non-ISAAC guidelines	31
written questionnaire	39
video questionnaire	6

*ISAAC – The International Study of Asthma and Allergies.

Many studies were conducted within one year (23 studies), sample sizes were mostly less than 1000 (mean 3243; median 2067), and study settings were predominantly mixed (urban and rural) (36 studies) (Table 3).

Prevalence estimates

We observed that the prevalence of asthma in some parts of Africa was comparable with that reported from surveys in high-income settings. From studies based on written questionnaires, "asthma ever" (cumulative prevalence of asthma) was highest in South Africa (53%, 5-12 years) in 1997 (20), followed by Egypt (26.5%, 11-15 years) in 2005 (52), Nigeria (18.4%, 15-35 years) in 1995 (45), and Ethiopia (16.3%, >20 years) in 1997 (73). The lowest prevalence was recorded in Gambia (1.9%, >15 years) in 1997 (69). "Current wheeze" (wheeze at rest-12-months) was consistently high in South Africa, 26.8% (13-14 years) in 1994, 23.9% (5-12 years) in 1998, and 20.3% (13-14 years) in 2003 (20,31,62). From studies based on video questionnaires, "current wheeze" was highest in Morocco (12.9%, 6-7 years) in 2003 (31) and Tanzania (12.3%, 9-10 years) in 2008 (35), with South Africa recording the lowest prevalence (6.5%, 6-7 years) in 1995 and 2000, respectively (31,62); there was no reported prevalence of "asthma ever" from studies based on video questionnaires. However, from all studies, the pooled crude prevalences (weighted means) for "current wheeze" was 13.2% (male 10.8%, female 13.1%, mean age 18.4 years), and "asthma ever" was 6.6% (male 6.7%, female 6.3%, mean age 22.9 years) (Table 4). We observed that the pooled crude prevalences were consistently higher among urban dwellers than rural dwellers. "Current wheeze" was 9.6% (male 12.1%, female 7.0%, mean age 19.6 years) in urban settings and 7.0% (male 5.5%, female 3.8%, mean age 17.5 years) in rural settings. "Asthma ever" prevalence was 5.9% (male 5.6%, female 3.9%, mean age 22.9 years) and 5.1% (male 4.2%, female 3.1%, mean age 17.5 years) in urban and rural dwellers, respectively (Table 5).

Our modeling revealed an increasing prevalence of asthma in Africa. We reported 34.1 million asthma cases (12.1%; 95% confidence interval [CI] 7.2-16.9) among children <15 years, 64.9 million asthma cases (11.8%; 95% CI 7.9-15.8) among people aged <45 years, and

74.4 million cases (11.7%; 95% CI 8.2-15.3) in the total population in 1990. This increased to 41.3 million (12.9%; 95% CI 8.7-17.0) among children <15 years, 82.4 million (12.5%; 95% CI 5.9-19.1) among people aged <45 years, and 94.8 million (12.0%; 95% CI 5.0-18.8) in the total population in 2000. In 2010, we estimated a total of 49.7 million asthma cases (13.9%; 95% CI 9.6-18.3) among children <15 years, 102.9 million (13.8%; 95% CI 6.2-21.4) among people aged <45 years, and 119.3 million cases (12.8%; 95% CI 8.2-17.1) in the total population. We could not model the asthma prevalences separately for men and women due to very limited data (Figure 2 and Table 6).

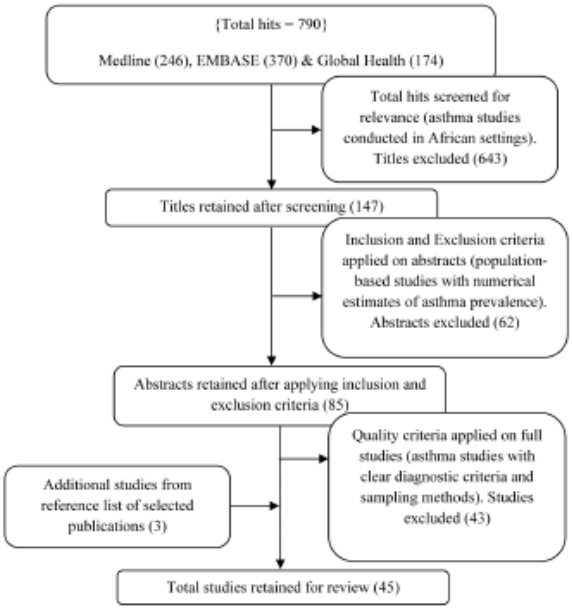

FIGURE 1. Search strategy.

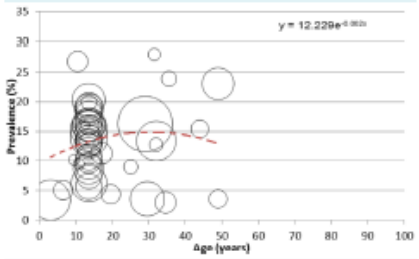

FIGURE 2. Age and prevalence distribution of asthma.

DISCUSSION

This study, to our knowledge, provides the first systematic, data-derived and continent-wide estimates of asthma prevalence in Africa. Our modeling was based on published epidemiological data on "current wheeze" prevalence, which has relatively higher sensitivity and specificity (1,17,30), and also shows a significant association between age and asthma prevalence (74).

From the 2010 Institute for Health Metrics and Evaluation (IHME) global burden of disease estimates, chronic respiratory diseases overall burden has been decreasing globally

and was responsible for about 4.7% of global disability adjusted life years (DALYs) in 2010, with asthma accounting for about one-fifth of this (75). However, the IHME reported that DALYs from asthma increased by 4.6% (from 21.5 to 22.5 million) between 1990 and 2010, while deaths decreased by 9.1% (from 0.38 to 0.34 million) over the same period globally (75,76). Concerns have been raised about the application of non-user friendly analytical methods, heavy statistical modeling, and difficulties in assessing the design methodologies and metrics used (77,78). In Africa however, the ISAAC study group, which mainly conducted epidemiological studies on asthma, reported increasing prevalences of asthma across many study settings (31). For example, the prevalence of "current wheeze" (wheeze at rest-12 months) among children aged 13-14 years old in South Africa increased from 16.1% to 20.3% between 1995 and 2002; Nigeria (West Africa) recorded an increase from 10.9% to 13.0%, Ethiopia (Horn of Africa) reported an increase from 6.2% to 9.1%, and Kenya (East Africa) an increase from 13.9% to 18.0% (31,32). Our pooled crude prev-

TABLE 4. Weighted mean prevalence (pooled crude prevalences) of asthma symptoms from all studies

		Overall study characteristics		All		Male		Female	
Study type	Asthma indices	study period	mean age (years)	data points	weighted mean % (95% confidence interval)	data points	weighted mean % (95% confidence interval)	data points	weighted mean % (95% confidence interval)
Written questionnaire	Asthma (ever)	1993-2008	22.9	50	6.6 (4.7-8.6)	6	6.7 (2.3-11.3)	6	6.3 (2.3-10.1)
	Wheeze at rest (12 mo)	1993-2010	18.4	46	13.2 (11.6-14.9)	7	10.8 (5.9-15.8)	7	13.1 (7.6-18.4)
	Wheeze at rest (ever)	1993-2010	14.7	12	17.7 (10.7-24.6)	2	9.1 (8.8-9.4)	2	6.2 (4.8-7.5)
	Wheeze after exercise (12 mo)	1995-2003	12.3	6	23.8 (15.9-31.7)	3	14.7 (4.4-33.8)	3	24.6 (11.0-38.2)
	Wheeze after exercise (ever)	1993-2010	12.0	11	8.9 (5.1-12.8)	1	6.5	1	6.5
	Nocturnal wheeze (12 mo)	1995-2005	15.4	6	4.9 (2.4-7.4)	1	9.1	1	10.0
	Nocturnal wheeze (ever)	-	-	-	-	-	-	-	-
	Nocturnal cough (12 mo)	1995-2005	14.1	7	24.2 (18.3-30.0)	3	24.5 (11.5-37.4)	3	28.1 (13.2-43.2)
	Nocturnal cough (ever)	1993	10.8	1	9.3	1	10.3	1	8.5
	Severe wheeze (12 mo)	1993-2003	13.1	25	4.7 (3.7-5.6)	4	6.0 (4.6-7.4)	4	3.0 (0.8-5.2)
	Severe wheeze (ever)	1993-2005	12.2	2	8.8 (5.9-11.6)	1	7.2	1	5.2
Video questionnaire	Wheeze at rest (12 mo)	1995-2008	13.0	9	9.7 (8.9-10.5)	1	11.7	1	13.0
	Wheeze at rest (ever)	1995-2008	13.1	8	13.2 (12.4-14.0)	1	16	1	18.2
	Wheeze after exercise (12 mo)	1995-2008	12.9	8	15.5 (14.7-16.3)	1	19.1	1	11.5
	Wheeze after exercise (ever)	1995-2008	13.0	7	20.4 (16.9-23.8)	1	28.7	1	15.4
	Nocturnal wheeze (12 mo)	1995-2008	13.0	8	5.6 (4.8-6.4)	1	9.6	1	5.1
	Nocturnal wheeze (ever)	1995-2008	13.0	8	8.1 (7.3-8.9)	1	14.9	1	19.2
	Nocturnal cough (12 mo)	1995-2008	12.9	8	17.7 (16.8-18.5)	1	22.3	1	20.5
	Nocturnal cough (ever)	1995-2008	13.0	7	24.6 (20.5-28.7)	1	31.9	1	34.6
	Severe wheeze (12 mo)	1995-2008	13.0	9	6.8 (6.1-7.6)	1	5.3	1	3.9
	Severe wheeze (ever)	1995-2008	13.1	8	9.6 (8.7-10.3)	1	12.8	1	13.0

TABLE 5. Rural and urban differences in asthma prevalences

		Study characteristics		All		Male		Female	
Asthma indices	Study setting	study period	mean age	data points	weighted mean % (95% confidence interval)	data points	weighted mean % (95% confidence interval)	data points	weighted mean % (95% confidence interval)
Asthma (ever)	Rural	1993-2008	17.5	6	5.1 (7.2-9.4)	2	4.2 (2.1-6.3)	2	3.1 (0.8-6.2)
	Urban	1993-2010	22.9	7	5.9 (2.9-7.9)	1	5.6	1	3.9
Wheeze at rest (12 mo)	Rural	1993-2008	17.5	6	7.0 (2.5-11.5)	2	5.5 (1.4-12.4)	2	3.8 (1.5-12.9)
	Urban	1993-2005	19.6	7	9.6 (3.9-15.2)	1	12.1	1	7

alences (weighted means) also reflect this increase; we reported a prevalence of current wheeze (wheeze at rest-12-months) of 13.2% for both written and video questionnaires respectively. Furthermore, in keeping with findings from many studies, our pooled crude prevalences were consistently higher in urban than rural settings, suggesting the effects of increasing urbanization on asthma prevalence in Africa (68,69,71).

From our modeling, we estimated a prevalence of 11.7% for asthma, totaling over 74 million people in 1990, and our 2010 prevalence was 12.8%, about 120 million people. Public health experts have reported that increasing tobacco smoking without appropriate legislation and implementation of relevant health promotional measures in many LMIC, especially in Africa, may also be responsible for the increase in asthma and other chronic respiratory diseases' burden in the region (2,75,79). In addition, the Global Burden of Asthma Report (GBAR) reported an increasing trend of asthma globally (4). GBAR estimated over 235 million asthma cases worldwide, and about 50 million people living with asthma in Africa in 2004, with the highest prevalence (8.1%) recorded in South Africa (4). The authors argue that this increasing trend is expected due to rise in atopic sensitizations, allergic conditions, and changing patterns of environmental triggers (associated with environmental smoking exposure in children, population growth, and urbanization) in Africa over the last two decades (4). These factors may therefore be indicative of our reported high estimates.

While we aimed to provide an improved prevalence estimate of asthma in Africa by carefully selecting high quality studies and applying simple analytical tools, there are however factors that could have affected our analysis. We thus entertain some degrees of uncertainties beyond the statistical confidence intervals generated, as variations in population settings, diagnostic criteria, sampling strategies, and effects of other health determinants (beyond age of patients) are factors that need be considered. First, the variation in diagnostic criteria was observed across many study settings, with criteria based on asthma symptoms and ISAAC scores frequently used. This could have reflected in our reported high estimates of asthma in Africa, as there is evidence suggesting the ISAAC studies could have over-estimated the prevalence of asthma in Africa, as most study centers were mainly urban (1); and with ISAAC studies conducted mainly in the age range 13-14 years, it may still not be representative of all age-groups and the overall population (1,15). Second, while many studies were cross-

TABLE 6. Estimated asthma cases and prevalences based on current wheeze "wheeze at rest- 12 months" (based on bubble graph and United Nations population estimates for Africa)

Age range(years)	1990 estimates (000)	2000 estimates (000)	2010 estimates (000)
0-4	13405.19	15750.21	18946.71
5-9	11202.33	13526.59	16412.34
10-14	9461.50	12041.26	14306.87
15-19	7889.99	10494.98	12758.85
20-24	6497.60	8806.244	11373.60
25-29	5391.37	7149.79	9722.56
30-34	4457.30	5804.15	7946.30
35-39	3648.13	4823.34	6315.71
40-44	2977.33	3998.62	5075.31
45-49	2409.99	3260.32	4208.92
50-54	2009.40	2627.89	3490.57
55-59	1637.07	2064.60	2801.72
60-64	1282.71	1638.11	2172.14
65-69	919.99	1226.50	1581.25
70+ years	1162.36	1593.05	2201.80
Asthma cases (<15 y)	34069.02	41318.06	49665.92
Estimated prevalence (<15 y)	0.121 (95%CI: 0.072-0.169)	0.129 (95%CI: 0.088-0.170)	0.139 (95%CI: 0.096-0.183)
Asthma cases (<45 y)	64930.74	82395.18	102858.20
Estimated prevalence (<45 y)	0.118 (0.079- 0.158)*	0.125 (0.059- 0.191)	0.138 (0.062- 0.210)
Asthma cases (all)	74352.26	94805.65	119314.60
Estimated prevalence (all)	0.117 (0.082- 0.153)	0.119 (0.050- 0.188)	0.128 (0.082- 0.171)

*CI – confidence interval.

sectional population-based, we also included studies conducted in occupational settings; this is in view of reports revealing that occupational asthma contributes significantly to the global burden of chronic respiratory diseases (73,80), and as these studies reported high prevalences, we understand this could have increased our estimates, too. Third, despite included studies spreading across most parts of Africa (24 countries in total), there are still many countries in Africa that are not included in the review; this reflects data gaps in the continent, and thus the generalizability of our estimates for Africa may need to be carefully examined. In addition, our overall sample size of 187 904 (from all studies) may not be a representative sample of the general African population as there were more younger age groups. Finally, data on age- and sex-specific prevalence, including corresponding data on urban-rural settings, which are vital comparative indices in any study, were not always provided across many studies.

Management of asthma and public health challenges in Africa

It is important to note that chronic respiratory disease burden, including asthma has continued to increase in Africa due to lack of appropriate response from the governments of many African countries (81,82). The national emphasis on asthma and relevant health messages have been sub-optimal, leading, in sequence, to poor awareness of the burden, low prioritization, inadequate staffing and resources, and very low budget allocation. In fact, budget allocation in many African countries mainly targets infectious diseases; funds have been greatly biased toward HIV/AIDS, malaria, and tuberculosis, as these are the main government priorities (28,83). The GBAR authors reported that poor government allocation of funds for asthma remained an important factor responsible for limited access to asthma medications, emergency health care, and other related health services in Africa (4). In addition, with tobacco companies still supporting many African governments, tobacco products' sales have increased, and government funds have remained unavailable for research on asthma, as researches aimed at improving management of asthma may be against tobacco sales and consumption (22,69). This has greatly resulted in increased smoking (without a counter legislation) and a growing burden of asthma, especially among children in Africa over the last two decades (5,10). For example, Mackay et al reported that a comprehensive smoke free-legislation was important to achieving reduction in the asthma incidence among people without occupational exposure to environmental tobacco smoke; a reduction of 18.2% per year was observed in hospital admissions in Scotland among children <15 years in 2009 compared to a mean increase of admission of 5.2% per year before implementation of the legislation in 2006 (84)

The diagnosis and treatment of asthma still remains a major challenge in Africa (16). Distinguishing asthma from other obstructive airway diseases has posed a clinical challenge to clinicians (3,5). Epidemiological data have shown that while asthma presents in episodes, usually among non-smokers and onsets before 40 years, chronic obstructive pulmonary disease (COPD) is associated with smokers, people aged 40 years and above, with symptoms being persistent and progressive (1). In practice, asthmatics who smoke may have non-reversible airflow limitation, and some COPD patients may be non-smokers having reversible airflow limitation (85). In addition, many African countries have no standard protocols for the diagnosis and management of asthma (22); where these are available, guidelines are rarely implemented, and for the few implemented guidelines, treatment often does not reach the rural population that is mostly affected (26). In fact, inaccessibility of health care services in many rural and resource-poor African settings often gives traditional healers undue significance in the management of many chronic diseases (22). The non-availability and unaffordability of inhaled steroids, and the relative non-adherence to these medications (when available) have also had large negative impact on the response to asthma in Africa. Studies have shown that about 50% of people adhere to prescribed medications (26,86), with reasons for non-adherence including side-effects, dosing frequencies, and lack of patient education on their illness, need for treatment, and how to take medications (87). There are also inherent socio-cultural misconceptions and individual values that need to be understood and addressed toward improving the acceptance and use of asthma medications (88), with continual public awareness and education being advocated, especially among parents of children with asthma (5,88).

Asthma is an important and increasing public health problem in Africa which receives inadequate priority and attention. With increasing urbanization, population aging, and adoption of western lifestyles in many African settings, these trends are set to continue in the near future. There is a need to identify and prioritize feasible strategies that can be adopted to promote the implementation of effective interventions that will address this increasing burden in Africa. There is also a need for African national governments to also consider effects of associated

risk factors in public health policy planning on this topic with a focus on reducing environmental triggers, placing restrictions on tobacco adverts, and appropriately educating health care personnel and the public on the management of the disease and the preventive measures.

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How big is the 'next big thing'?

Estimating the burden of non–communicable diseases in low– and middle–income countries

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Non-communicable causes of death and disability will dominate global health agenda for the foreseeable future. The progress in addressing their burden and achieving measurable reduction in low– and middle–income countries (LMICs) will likely require similar steps that were effective in reducing maternal and child mortality globally: (i) defining the size of the burden and the main causes responsible for the majority of the burden; (ii) understanding the most important risk factors and their importance in different contexts; (iii) systematically assessing the effectiveness and cost of the interventions that are feasible and available in LMICs; and (iv) formulating evidence–based health policies that will define appropriate health care and health research priorities to tackle the burden in the most cost–effective way.

Over the past year the pandemic of non–communicable diseases (NCDs) has become a key focus of global political agenda. At the United Nations' high–level meeting on the prevention and control of NCDs in September 2011, a general consensus has been reached that NCDs were already the leading causes of death in all world regions and that their burden is increasing rapidly [1]. The rate of this increase is particularly striking in low– and middle–income countries (LMICs), where life expectancy is increasing as a result of improved socio–economic conditions [2]. It is expected that by the year 2030, NCDs could become responsible for 52 million deaths [3]. In LMICs, health systems will face considerable challenge in adjusting to the rapidly growing demand for services, and this could in turn become an additional significant barrier to achieving the Millennium Development Goals [2]. As a result, many parallel advocacy efforts for tackling NCDs are taking place, with a particular focus on heart disease, cancer, respiratory diseases, diabetes and stroke [4]. A number of interventions have been outlined that could have immediate preventive effect and slow down the pandemic, such as tobacco control, improved diet, exercise and decreased alcohol intake [4].

The release of the new global burden of disease (GBD) estimates for the year 2010, by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington in Seattle, is anticipated with great interest [5]. The new revision is expected to show substantial progress in the reduction of maternal and child mortality in the LMICs over the past two decades. However, many fear that there will be hardly any measurable progress in improving health and survival of adult populations in LMICs. The UN conference in 2011 and the publication of the new GBD estimates could therefore mark the beginning of the era in which non–communicable causes of death and disability will dominate global health agenda for the foreseeable future. The progress in addressing their burden and achieving measurable reduction in LMICs will likely require similar steps that were effective in reducing maternal and child mortality globally: (i) defining the size of the burden and the main causes responsible for the majority of this burden; (ii) understanding the most important risk factors and their importance in different contexts; (iii) systematically assessing the effectiveness and cost of the interventions that are feasible and available within the contexts of different LMICs; and (iv) formulating evidence–based health policies that will define appropriate health care and health research priorities to tackle the burden in the most cost–effective way.

Measuring the burden of non–communicable diseases in low–resource settings is a challenging task given the scarcity of available data, inconsistency in case definitions of the measured diseases, differences in reporting of results used by different investigators, lack of funding, research infrastructure and capacity for community–based studies, changing definitions of diseases over time, low transcultural adaptability of screening instruments, and many others.

The first step in this process is to measure the burden of NCDs in LMICs. This is a challenging task given the scarcity of available data, inconsistency in case definitions of the measured diseases, differences in reporting of results (eg, age groups) used by different investigators, lack of funding, research infrastructure and capacity for community–based studies in LMICs, changing definitions of diseases over time, low transcultural adaptability of screening instruments, and many others [6-8]. Methodological approaches that could take into account the diversity and scarcity in the available information and produce acceptable regional estimates using transparent and sound methodological approaches are urgently needed. Furthermore, the international research community could benefit from clear guidelines on conducting epidemiological studies in LMICs that could inform burden of disease analyses, so that research results are comparable and leading to more reliable estimates.

In the current issue of the *Journal of Global Health*, we are publishing several studies that attempt to summarise information on the burden of non–communicable diseases and provide estimates for a region that has traditionally been considered "information gaps": the African continent. The papers by George-Carey et al. [9], Paul et al. [10], Graham et al. [11] and Dowman et al. [12] provide the first systematic estimates of the burden of dementia, epilepsy and rheumatoid arthritis, respectively. In addition, Reidpath and Allotey provide an authoritative viewpoint on the changing chronic disease management in LMICs [13], Moten et al. discuss the challenge of equitable building of public health infrastructure in low resource settings [14], Kolcic warns of the "double burden of malnutrition" as a silent driver of the NCD pandemic [15], while Maher and Sridhar address the role of political priority in the global fight against NCDs [16]. In the future issues of our journal, we will increasingly welcome similar attempts to quantify disease burden, the role of risk factors and the effectiveness of interventions targeted at reducing NCDs in low resource settings.

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An estimate of the prevalence of hypertension in Nigeria: a systematic review and meta-analysis

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Background: Hypertension is a leading cause of morbidity and mortality in Africa, and Nigeria, the most populous country in the continent, hugely contributes to this burden.

Objective: To provide an improved estimate of the prevalence and number of cases of hypertension in Nigeria based on the cut-off 'at least 140/90 mmHg', towards ensuring better awareness, control and policy response in the country.

Methods: We conducted a systematic search of Medline, EMBASE and Global Health from January 1980 to December 2013 for population-based studies providing estimates on the prevalence of hypertension in Nigeria. From the extracted crude prevalence rates, we conducted a random-effects meta-analysis, and further estimated the overall awareness rate of hypertension in Nigeria, expressed as percentage of all hypertension cases. We applied a meta-regression epidemiological modelling, using United Nations population demographics for the years 2010 and 2030, to determine the prevalence and number of cases of hypertension in Nigeria for the 2 years.

Results: Our search returned 2260 publications, 27 of which met our selection criteria. From the random-effects meta-analysis, we estimated an overall hypertension prevalence of 28.9% (25.1, 32.8), with a prevalence of 29.5% (24.8, 34.3) among men and 25.0% (20.2, 29.7) among women. We estimated a prevalence of 30.6% (24.5, 36.6) and 26.4% (19.4, 33.4) among urban and rural dwellers, respectively. The pooled awareness rate of hypertension was 17.4% (11.4, 23.3). The overall mean SBP was 128.6 (125.5, 130.8) mmHg, and the DBP was 80.6 (78.5, 82.7) mmHg. From our modelling, we estimated about 20.8 million cases of hypertension in Nigeria among people aged at least 20 years in 2010, with a prevalence of 28.0% (24.6, 31.9) in both sexes – 30.7% (24.9, 33.7) among men and 25.2% (22.7, 31.9) among women. By 2030, we projected an increase to 39.1 million cases of hypertension among people aged at least 20 years with a prevalence of 30.8% (24.5, 33.7) in both sexes – 32.6% (27.3, 38.2) among men and 29.0% (21.9–32.2) among women.

Conclusions: Our findings suggest the prevalence of hypertension is high in Nigeria, and the overall awareness of raised blood pressure among hypertension cases is low in the country. We hope this study will inform appropriate public health response towards reducing this burden.

Keywords: Africa, burden, cardiovascular disease, hypertension, Nigeria, prevalence

Abbreviations: DALYs, Disability-Adjusted Life Years; ICSHIB, International Collaborative Study of Hypertension in Black; ISH, International Society of Hypertension; JNC, Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure; LMIC, low and middle-income countries; MESH, Medical Subject Headings; NCDs, non-communicable diseases; UN, United Nations; USD, United States dollars

INTRODUCTION

The burden of non-communicable diseases (NCDs), including hypertension, is fast rising globally, and reports from the 2013 World Health Day global brief on hypertension shows that Africa, in particular, is worst hit [1]. WHO, public health experts and stakeholders have declared NCDs a global priority, as documented in the 2011 United Nations (UN) high-level meeting, with a target towards reducing this growing burden in Africa and other low and middle-income countries (LMICs) [2], where an existing burden from many infectious diseases has contributed to a double burden of disease [3].

Hypertension is estimated to affect about one billion people worldwide and is a major risk factor for many cardiovascular diseases [1]. Cardiovascular diseases are responsible for about 17 million deaths globally, with

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complications from high blood pressure resulting in about 7.5 million deaths and 57 million disability-adjusted life years (DALYs) worldwide, both accounting for about 12.8 and 3.7% of global deaths and DALYs, respectively [1,4]. Nigeria, currently with a population of over 160 million, is the most populous African country [5], and the prevalence of hypertension in the country hugely contributes to the overall burden in Africa [6]. In 2008, the WHO estimated hypertension prevalence of 42.8% in Nigeria [7]. This is believed to be due to an increasing adult population, rapid urbanization and uptake of western lifestyles, including high consumption of processed foods (with high salts and fats), tobacco and alcohol products [8,9].

The 1997 Nigerian national NCDs survey committee reported a hypertension prevalence of 11.2% in both sexes, which was then about 4.33 million hypertension cases in people aged above 15 years [10]. This survey could have underestimated the prevalence of hypertension in Nigeria, as the diagnosis was based on the old definition of hypertension (≥160/95 mmHg) [8,11]. From the 2003 national NCDs survey conducted mainly in the south-west region, which was based on SBP at least 140 mmHg and/or DBP at least 90 mmHg, the overall prevalence of hypertension was 28.9% [12]. In addition, recent surveys in various parts of Nigeria based on at least 140/90 mmHg have also shown a higher prevalence of hypertension, ranging from 25.0 to 36.6% [9].

One major problem affecting the response to this burden in Nigeria is that the awareness, treatment and control of hypertension have been low [13]. Consequently, many who live with high blood pressures end up in health facilities with cardiovascular complications, including heart failures, ischemic heart disease and strokes [14]. In fact, research findings show that high blood pressure is diagnosed in many people as an incidental finding when admitted for unrelated ailments [15]. This obviously has resulted in high morbidities and mortalities from hypertension in Nigeria [3], and reports still show that there is yet to be a nationwide measure to facilitate regular screening and detection of high blood pressures [8,16,17]. The WHO reiterated the need for improved awareness on high blood pressure towards reducing the overall burden of the disease, especially at national and community levels, as this was the focus of the 2013 WHO day [1]. Additionally, there is also a high economic burden as a consequence of hypertension and associated cardiovascular complications in Nigeria [18], demonstrated by direct costs, for example: the cost of antihypertensive medications, administrative fees, laboratory fees and other out-of-pocket health expenditures, and indirect costs, such as: loss of savings from repeated healthcare expenses, hospital waiting times and work absenteeism [19]. In a study of 250 patients in Igbo-Ora, southwest Nigeria, for instance, the mean monthly cost of treatment was reported to be about 10 United States Dollars (USD) and this is relatively high in a community in which majority of the population live on an income below 2 USD per day [20]. Furthermore, some reports have shown that the actual mean monthly cost could be more than this, as the study did not consider re-treatment visits which could be up to five visits per patient within 6 months [19].

The burden of hypertension in Nigeria is high and still growing [8], and we still cannot say with certainty the exact burden. In the past 20 years, there has been an increase in hypertension research in Nigeria, as several community-based prevalence studies have been conducted [21]. There is therefore a need for current estimates of the prevalence of hypertension in the country to effectively quantify this burden and prompt appropriate response as previous countrywide estimates have been based on a review of fewer studies, mostly based on at least 160/95 mmHg [21]. The aim of this study was to provide an improved estimate of hypertension in Nigeria, based on the current definition (cut-off '≥140/90 mmHg') [22–25], towards ensuring improved awareness, control and treatment, and a better policy response.

METHODS

Search strategy and selection criteria

After identification of the relevant Medical Subject Headings (MESH) and keywords, a final search strategy was developed. Searches were conducted in three main databases: Medline, EMBASE and Global Health. The search date was set from January 1980 to September 2013, as studies conducted after 1980 broadly reflect the introduction of hypertension definition based on at least 140/90 mmHg, which is our broad diagnostic criteria (see 'Case definitions' section below). See Table 1 for details of the search terms.

We included cross-sectional population and/or community-based studies on hypertension published in or after 1980, conducted among people aged at least 15 years, and providing numerical estimates on the prevalence or awareness rates of hypertension in Nigeria. We excluded studies conducted before 1980, hospital-based, without numerical estimates, on non-human participants, and that were mainly reviews. We also ensured the retained studies had clearly defined study designs, diagnostic criteria and blood pressure measurement protocols.

TABLE 1. Search terms

#	Search terms
1	nigeria/ or 'africa south of the sahara'/
2	Nigeria .mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
3	1 or 2
4	exp vital statistics/ or exp incidence/
5	(incidence* or prevalence* or morbidity or mortality).tw.
6	(disease adj3 burden).tw.
7	exp 'cost of illness'/
8	exp quality-adjusted life years/
9	QALY.tw.
10	Disability adjusted life years.mp.
11	(initial adj2 burden).tw.
12	exp risk factors/
13	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14	cardiovascular diseases/ or heart diseases/ or exp hypertension/ or peripheral vascular diseases/
15	Hypertensive heart disease.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
16	14 or 15
17	3 and 13 and 16
18	limit 17 to (humans and yr="1980 -Current")

Case definitions

We included studies with hypertension defined as: SBP at least 140 mmHg and/or DBP at least 90 mmHg. To satisfy this definition, included studies needed to comply with the hypertension diagnostic criteria based on the following: the sixth and seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC6 and JNC7) [22,23], the 1999 WHO/International Society of Hypertension (WHO/ISH) definitions and classification of blood pressure levels [24], and the 2003 WHO/ISH Statement on Management of Hypertension [25]; as these criteria all have their hypertension cut-off based on 140/90 mmHg. However, many studies before 1999 were based on different blood pressure classifications (with hypertension mostly defined as ≥160/95 mmHg). For these studies, we extracted any subgroup analysis based on our initial definition and calculated the hypertension prevalence only from this subgroup. Thus, all included studies were finally based on SBP (≥140 mmHg) and/or DBP (≥90 mmHg).

For the awareness rate of hypertension, we included studies estimating the prevalence of hypertension based on the above definition, with awareness rate of hypertension defined as self-report by respondents of any prior diagnosis of hypertension by a doctor or a certified health worker, and excluding women diagnosed during pregnancy [25].

Data extraction and analysis

All extracted data were stored in the Microsoft Excel file format. The data were abstracted systematically on sample size, mean age or age range, number of hypertension cases, and their respective age and sex-specific prevalence rates. These were sorted into mixed, urban and rural settings (based on studies that reported them). An independent parallel search and double extraction was conducted by C.B. and A.V.A., respectively. For studies conducted on the same study site, population or cohort, the first chronologically published study was selected, and all additional data from other studies were compared for consistency and included in the selected study.

As noted above, awareness of hypertension was defined as the number of people who reported being aware of their hypertension status. From each study, the awareness rate of hypertension was estimated as the number of people who reported being hypertensive, expressed as a percentage of total number of people in the study population adjudged to have hypertension. Pooled awareness rate of hypertension (relative to the sample size of the study population) was then estimated using a random-effects meta-analysis (DerSimonian and Laird method) [26].

We further conducted a random-effects meta-analysis on crude hypertension prevalence rates from all study sites, and separately pooled estimates for urban and rural settings. We further conducted a meta-regression-like analysis on all data points, employing an epidemiological model adjusted for mean ages, with the size of bubble corresponding to the reported sample sizes in each study, and the fitted curve explaining the largest proportion of variance (best fit) was applied. Data from studies conducted before 2010 were used to estimate the prevalence and cases of hypertension in 2010. The equations generated from the fitted model were then separately used to estimate the number of cases of hypertension at midpoints of the UN population 5-year age groups for the year 2010 [27]. This epidemiological model has been described in two previous studies [28,29]. To give a close prediction of the prevalence of hypertension in Nigeria in 2030 with appropriate consideration of the expected population growth and ageing in the country, we modelled all data extracted from the remaining studies (representing the period 2010–2013) to arrive at these predicted estimates, as the UN population figures were also partly extrapolated from the projected population growth and ageing. All statistical analyses were conducted on Microsoft Excel and Stata 13.1 (Copyright 1985–2013 Stata Corp LP).

RESULTS

Systematic review

Our search returned 2260 publications from Medline (551), EMBASE (710) and Global Health (999). A further 4 studies were included from other sources. 1908 studies remained after removing duplicates. On screening titles for relevance (i.e. hypertension studies conducted primarily on Nigerian populations), 1769 studies were excluded. We therefore assessed 139 full texts, and after applying the quality criteria, 112 studies were excluded [56 articles did not provide numerical estimates for prevalence and cases of hypertension, 47 articles did not specify study designs and blood pressure measurement protocols, and 9 studies were based on a cut-off of ≥160/95 mmHg (without any group estimate based on 140/90 mmHg)]. A total of 27 studies were finally retained for the review (see Fig. 1 for flow diagram of study selection).

Study characteristics

The 27 studies [30–56] were conducted across the six geopolitical zones of Nigeria (south-west 10, south-east 7, south-south 6, north-central 2, north-east 1, north-west 1), with most studies (88%) completed within 1 year (see Table 2). The overall sample size from all retained studies was 27 122, with a mean and median of 1005 and 756, respectively. Of the 27 studies, 21 reported hypertension prevalence estimates by sex. The total sample size of the male population was 10 759 (mean 512) and that of the female population was 10 297 (mean 490). Fourteen studies (51.9%) were conducted in predominantly urban settings, with a total sample size of 11 726 (mean 838). Studies from rural settings were seven, whereas studies conducted in mixed settings (which describe a study conducted across both urban and rural settings, with a single prevalence estimate reported for this setting) were six in all. Many studies applied the JNC7 and WHO/ISH 2003 hypertension classifications, both representing about 45% of all criteria used. The studies were mostly conducted on people aged at least 20 years, with an estimated overall mean age of 45.1 years, ranging from 30.7 to 71.1 years. For the age determination of patients across selected studies, birth certificates were mostly employed, and in the absence of valid age-verification documents, patients' age was determined from historical landmarks.

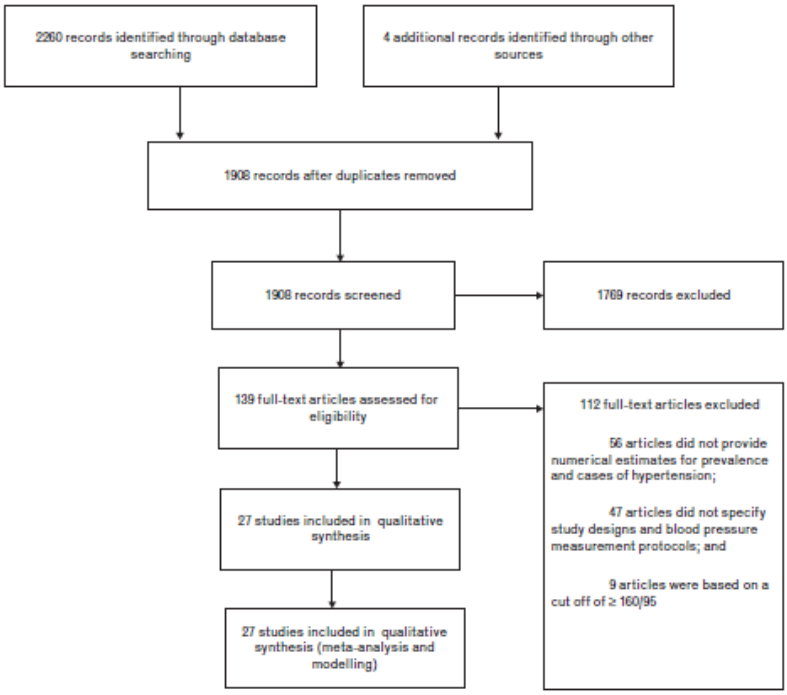

FIGURE 1 Flow chart of study selection.

Pooled estimates

On the basis of reported prevalence rates in individual studies, the highest prevalence of hypertension was recorded in Ogbomoso (south-west Nigeria) and Abak (south-south Nigeria), both having a prevalence of 50.5% in 2008 (mean age 48.7 years) and 47% in 2012 (mean age 31.7 years), respectively [35,41]. Other sites reporting a high prevalence of hypertension were from Enugu (south-east Nigeria), with a prevalence of 44.5% in 2011 (mean age 57.3 years), 46.4% in 2006 (mean age 59.8 years) and 42.2% in 2010 (mean age 38.0 years) [37,40,56]. Across all study sites, lowest hypertension prevalence was reported in Ibadan (south-west Nigeria) with a prevalence of 9.3% in 2008 (mean age 38.3 years) [46] (see Table 3 for summary of data from all retained studies).

TABLE 2. Characteristic distribution of selected studies

	Number of studies
Study location (according to the 6 geopolitical zones of Nigeria)	
South-west [30,31,34–36,39,43,46,48,51]	10
South-east [37,40,42,47,49,55,56]	7
South-south [33,38,41,52–54]	6
North-central [44,50]	2
North-east [32]	1
North-west [45]	1
Duration of study	
<1 year	23
1–3 years	4
>3 years	0
Sample size	
<1000	17
1001–3000	10
>3000	0
Study setting	
Rural	6
Urban	14
Mixed[a]	7

[a]Mixed setting refers to a study conducted across both urban and rural settings, with a single prevalence estimate reported for this setting.

From the random-effects meta-analysis conducted on all data points, we estimated an overall hypertension prevalence of 28.9% [95% confidence interval (CI) 25.1–32.8, $I^2 = 98.2\%$, $P = 0.000$), with men having 29.5% (95% CI 24.8–34.3, $I^2 = 96.8\%$, $P = 0.000$) and women having 25.0% (95% CI 20.2–29.7, $I^2 = 97.2\%$, $P = 0.000$). The pooled prevalence of hypertension in the urban settings was higher than that in the rural settings. We estimated prevalence rates of 30.6% (95% CI 24.5–36.6, $I^2 = 96.8\%$, $P = 0.000$) among the urban dwellers, and 26.4% (95% CI 19.4–33.4, $I^2 = 96.8\%$, $P = 0.000$) among the rural dwellers (Table 4 and Figs. 2–4).

From all studies reporting mean blood pressures, the overall pooled estimates (random-effect meta-analysis) of

TABLE 3. Summary of data from all studies

Author, year (location, setting)	Study period	Diagnostic criteria	Mean age in years (all)	Prevalence % (all)	Prevalence % (men)	Prevalence % (women)
Abegunde and Owoaje, 2013 (Oyo, South-west, mixed) [30]	2010–2011	JNC7	71.1	34.8	–	–
Adedoyin *et al.*, 2008 (Ile-Ife, south-west, semi-urban) [31]	2007–2008	JNC7	44.2	36.6	36.8	36.4
Adedoyin *et al.*, 2012 (Borno, north-east, semi-urban) [32]	2011–2012	JNC7, WHO/ISH 2003	41.5	25.2	24.7	24.7
Ahaneku *et al.*, 2011 (Enugu, south-east, rural) [37]	2010–2011	≥140/90	57.3	44.5	49.3	42.3
Alikor *et al.*, 2013 (Rivers, south-south, rural) [33]	2012–2013	JNC7	41.3	20.2	20.5	20.1
Amira *et al.*, 2012 (Lagos, south-west, urban) [34]	2006–2010	JNC7	41.9	33	38.3	27.8
Amole *et al.*, 2011 (Ogbomoso, south-west, semi-urban) [35]	2008	JNC7	48.7	50.5	52	49.3
Asekun-Olarinmoye *et al.*, 2013 (Osun, south-west, rural) [36]	2011	JNC7, WHO/ISH 2003	49.7	13.2	15	11.9
Bunker *et al.*, 1992 (Benin, south-south, urban) [38]	1987–1988	≥140/90	36.35	31.1	34	17
Cooper *et al.*, 1997 (Ibadan, south-west, mixed) [39]	1995	≥140/90	49.5	14.5	14.7	14.3
Ejim *et al.*, 2011 (Enugu, south-east, rural) [40]	2005–2006	≥140/90	59.8	46.4	50.2	44.8
Ekanem *et al.*, 2013 (Abak, south-south, semi-urban) [41]	2012	JNC7	31.7	47	30.1	16.8
Ekwunife *et al.*, 2010 (Nsukka, south-east, mixed) [42]	2009	≥140/90	34.9	21.1	–	–
Erhun *et al.*, 2004 (Ile-Ife, south-west, semi-urban) [43]	2002–2003	JNC6, WHO/ISH 1999	55	21	23.3	16.4
Hendriks *et al.*, 2012 (Kwara, north-central, rural)	2009–2011	≥140/90	45.3	21	–	–
Isezuo *et al.*, 2011 (Sokoto, north-west, mixed) [45]	2009–2010	JNC7	38.9	24.8	25.9	23.6
Kadiri *et al.*, 1999 (Ibadan, south-west, urban) [46]	1997–1998	≥140/90	38.3	9.3	10.4	7.1
Mbah *et al.*, 2013 (Nsukka, south-east, semi-urban) [47]	2011–2012	JNC7	50	32.5	–	–
Odugbemi *et al.*, 2012 (Lagos, south-west, urban) [48]	2009–2010	≥140/90	43.885	34.8	–	–
Ogah *et al.*, 2013 (Abia, south-east, mixed) [49]	2011–2012	JNC7	41.7	31.8	33.5	30.5
Oghagbon *et al.*, 2008 (Ilorin, north-central, urban) [50]	2006–2007	WHO/ISH 2003	50.5	27.1	28.4	22.9
Oladapo *et al.*, 2010 (Egbeda, south-west, rural) [51]	2002–2005	JNC7	42.1	20.8	21.1	20.5
Omorogiuwa *et al.*, 2009 (Ekpoma, south-south, urban) [52]	2007–2008	≥140/90	41.6	33	28.1	36.4
Omuemu *et al.*, 2007 (Edo, south-south, rural) [53]	2004–2005	WHO/ISH 2003	30.7	20.2	24.8	13.2
Suleiman *et al.*, 2013 (Amasomma, south-south, semi-urban) [54]	2011	JNC7	50.5	15	18.8	12.5
Ulasi *et al.*, 2010 (Enugu, south-east, Semi-urban) [55]	2007–2008	WHO/ISH 2003	40.8	32.8	–	–
Ulasi *et al.*, 2011, Enugu, south-east, mixed) [56]	2009–2010	WHO/ISH 2003	38.02	42.2	46.3	37.7

JNC, Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure [22,23], ISH, International Society of Hypertension [24,25].

SBP and DBP were 128.6 (125.5, 130.8) mmHg and 79.4 (78.5, 82.7) mmHg, respectively (Table 4 and Fig. 5).

On the basis of our definition of awareness of hypertension, only six studies satisfied this definition (percentage of people with hypertension who were aware of their hypertension status). The pooled hypertension awareness rate (random-effect meta-analysis) was 17.4% (11.4, 23.3) (Table 4 and Fig. 6).

Modelled estimates

Our modelling showed the overall cases and prevalence of hypertension were high in Nigeria. We estimated about 20.8 million cases of hypertension in Nigeria among people aged at least 20 years in 2010, with a prevalence of 28.0% (24.6, 31.9). Just as observed from the crude estimates (meta-analysis), the prevalence of hypertension among men was higher than that among women. We estimated over 11.4 million cases of hypertension with a prevalence of 30.7% (24.9, 33.7) among men, and 9.3 million cases with a prevalence of 25.2% (22.7, 31.9) among women (Table 5 and Fig. 7 for details). We projected an increase to about 39.1 million cases of hypertension by 2030 in people aged at least 20 years, with a prevalence of 30.8% (24.5, 33.7). Among men, we projected an increase to over 20.7 million cases with a prevalence of 32.6% (27.3, 38.2), and an increase to about 18.3 million cases with a prevalence of 29.0% (21.9, 32.2) among women. These projections are mainly based on expected population growth and ageing of the Nigerian population by the year 2030 (Table 6 and Fig. 8 for details).

TABLE 4. Pooled hypertension prevalence rates from all studies

Setting	Mean age (years)	Prevalence and awareness rates of hypertension (%)				Mean blood pressure (mmHg)	
		Both sexes[a] (95% CI)	Men[a] (95% CI)	Women[a] (95% CI)	Awareness rate (95% CI)	SBP (95% CI)	DBP (95% CI)
Overall[b]	45.1	28.9 (25.1, 32.8)	29.5 (24.8, 34.3)	25.0 (20.2, 29.7)	17.4 (11.4, 23.3)	128.6 (125.5, 130.8)	80.6 (78.5, 82.7)
Mixed	45.7	28.1 (19.6, 36.7)	29.9 (17.2, 42.8)	26.4 (15.9, 36.9)	–	–	–
Urban	44.1	30.6 (24.5, 36.6)	29.4 (22.6, 36.2)	24.3 (16.7, 31.8)			
Rural	46.9	26.4 (19.4, 33.4)	29.6 (19.9, 39.3)	25.3 (15.1, 35.5)			

Mixed setting refers to a study conducted across both urban and rural settings, with a single prevalence estimate reported for this setting (see Table 4 for more details). CI, confidence interval.
[a]Hypertension prevalence.
[b]Estimates are from all data points.

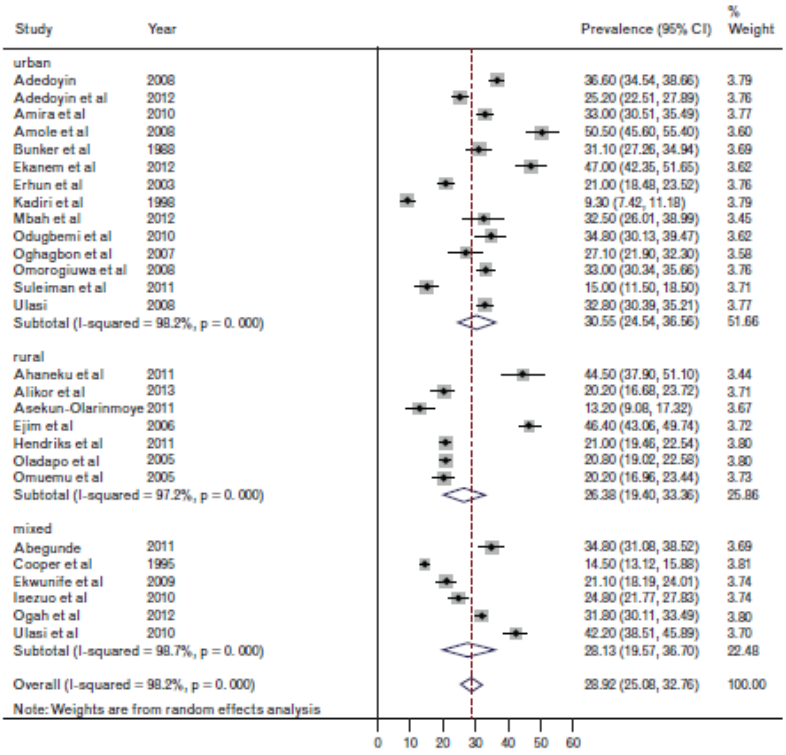

FIGURE 2 Forest plot of crude hypertension prevalence rates in both sexes in Nigeria.

DISCUSSION

There are clear indications of the need for an estimate of hypertension in Nigeria [21], as a countrywide hypertension prevalence was last estimated in Nigeria during the 1997 national survey of NCDs [10], and a follow-up done in 2003 was inconclusive and limited only to south-western Nigeria [12]. There has been a gradual increase of community-based studies from various sites within the country in the past two decades using the recent WHO/ISH and JNC7 definitions, and most reporting higher prevalence rates of hypertension [8,21]. We therefore believe a countrywide estimate of hypertension prevalence by systematically selecting the relevant studies (vis-à-vis standard diagnostic criteria and blood pressure-measuring protocols) may help address pertinent health challenges, prompt more research efforts and inform appropriate public health response. This review thus provides an improved countrywide estimate of the prevalence of hypertension in Nigeria for the years 2010 and 2030, using an epidemiological model adjusted for age and sample sizes of the study populations.

We estimated overall mean SBP and DBP of 128.6 and 80.6 mmHg in Nigeria. This, to the best of our knowledge, is the first countrywide estimate of SBP and DBP in Nigeria. This estimate is relatively comparable with the estimates reported for sub-Saharan Africa between 1981 and 2008 by Danaei *et al.* [57], with an overall mean SBP ranging from 129.2 to 132.7 mmHg and 132.6 and 134.8 mmHg among men and women, respectively. This may broadly reflect an increasing overall mean blood pressure and a rising prevalence of hypertension in the country when compared to other world regions [58]. From the pooled crude prevalence rates, we observed that the prevalence of hypertension was higher among the urban dwellers than that observed among the rural dwellers (31 versus 26%). This is in line with several studies in Nigeria and other contextually comparable African countries where a higher prevalence of hypertension has been reported among the urban dwellers [59]. For example, in 2008, a prevalence of 22.3% was estimated among the urban dwellers in Nigeria as compared to a prevalence of 15.0% among the rural dwellers [60]. This may possibly reflect intense physical activities from long walking hours and rigorous farming in most rural places, coupled with better consumption of locally available fruits and vegetables, and a probable absence of western lifestyles [61,62].

One important finding from this study is the low rate of awareness on hypertension. We reported a pooled

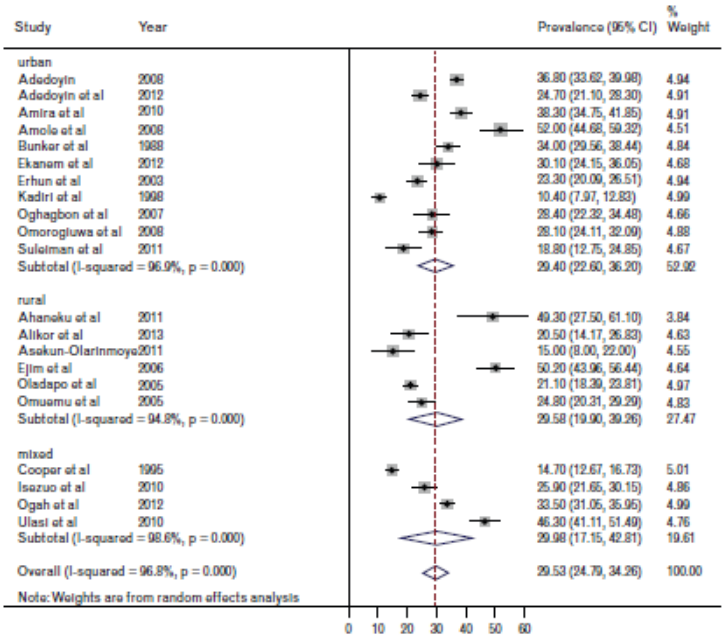

FIGURE 3 Forest plot of crude hypertension prevalence rates among men in Nigeria.

awareness rate (expressed as a percentage of cases of hypertension) of 17.4% (11.4, 23.3) in Nigeria. This also remains the first countrywide estimate of awareness rate of hypertension in Nigeria. This awareness rate is relatively in line with reports from many studies in other parts of Africa (Gabon 9%, Uganda 10% and Kenya 12.3%) [63–65]. This may be indicative of the high morbidities and mortalities from hypertension and associated complications in many African regions [6]. Reports show that addressing hypertension awareness by instituting regular community checks of blood pressure is cost-effective and may help reduce cardiovascular complications from hypertension in many resource-poor settings [66].

From our modelling, we estimated about 20.8 million hypertensive cases among people aged at least 20 years in 2010, with a prevalence of 28.0% in both sexes, and men having higher prevalence (30.7%) than women (25.2%). Our prevalence is higher than was previously reported in the 1997 survey, which was based on at least 160/95 mmHg (11.4%) [10]. Twagirumukiza *et al.* [60] reported a prevalence of 18.4% (men 19.4%, women 17.5%) among people aged at least 15 years in Nigeria in 2008. This is quite low compared to our estimates, and may be due to the fact that the prevalence reported for Nigeria was based on a logistic model applied on a single study conducted in south-western Nigeria in 1999, and may therefore not be representative of the overall Nigerian population in 2008 [60,67]. This may also be similar with the prevalence reported by the International Collaborative Study of Hypertension in Blacks (ICSHIB) in 1995, where an age-adjusted prevalence of hypertension in Nigeria was estimated as 14.5% (14.7% for men and 14.3% for women) [39]. This estimate was also based on a small population group (sample size 1171), and their age-adjusted estimate may not be representative of the overall Nigerian population.

Some recent estimates were reported by Ogah *et al.* [21] with a prevalence of 22.5% for the period 2000–2009, and Ekwunife and Aguwa [68] estimated a prevalence of 22% for the period 1990–2009. These estimates are relatively low in comparison to our current estimates. As noted above, the prevalence reported by Ekwunife and Aguwa may also not be representative of the entire Nigerian population as it was derived from nine studies mainly conducted in south-western Nigeria [68]. However, Ogah *et al.* did review more studies (30 studies), but these studies were selected from 1960 (a period when hypertension was not yet based on cut-off of 140/90 mmHg), and the hypertension criteria used by the authors were not explained in detail.

Meanwhile, the observed higher prevalence in men has also been reported by many African studies having similarities with Nigeria [59]. This may be because the overall mean age from all selected studies was 45.1 years, which is just about a reported 49.4 years mean menopause age among Nigerian women [69], and there is established evidence of a steeper blood pressure increase in men than women before the age of menopause [70]. It may also be linked to socio-economic factors, where men are mostly responsible for family maintenance and finances, and are

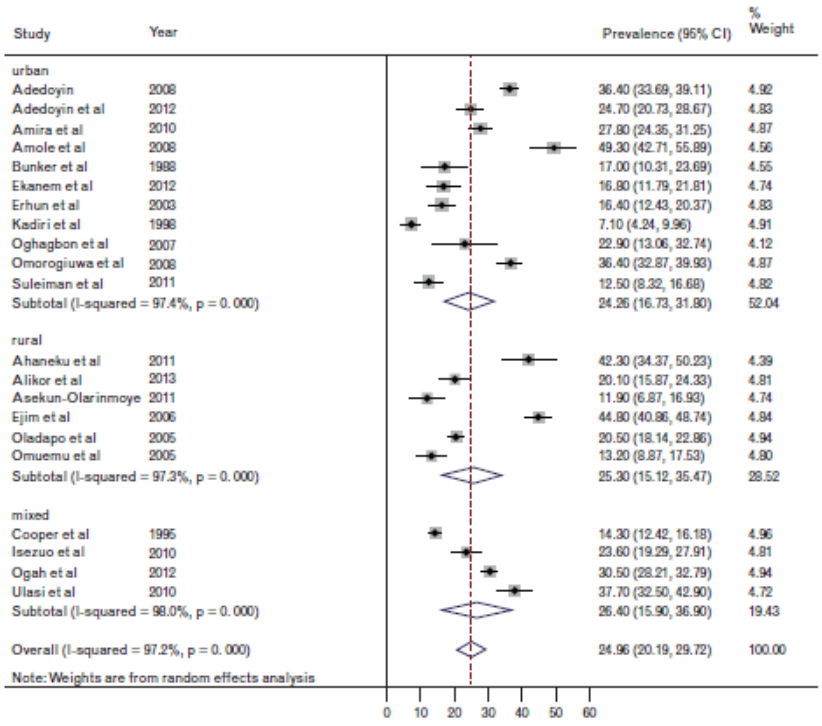

FIGURE 4 Forest plot of crude hypertension prevalence rates among women in Nigeria.

unduly stressed by the need to fulfil these obligations [8]. However, the prevalence reported by the WHO global status report on NCD groups was higher at 42.8% for both sexes, 41.5% in men and 44.0% in women among people aged at least 25 years [7]. There are still concerns over the sources of data and type of modelling used, as experts have reported a possible over-estimation of the prevalence from a rather sophisticated statistical modelling [71,72]; we may therefore need to interpret this with caution.

Our 2030 projections show an increase in hypertension cases and prevalence from the 2010 estimates. With emerging new families gradually adopting smaller family sizes in Nigeria, we assumed there would be no huge difference in fertility rate in Nigeria by 2030. We thus employed the constant fertility variant of the United Nations population projections for Nigeria in 2030 to arrive at our projected number of hypertension cases and prevalence [27]. Our projected increase is a reflection of the overall population growth and ageing in the country, with the absolute number of cases of hypertension almost doubling from 20.8 million in 2010 to 39.1 million in 2030. However, with a marginal increase in prevalence from 28.0 to 30.8%, this may be due to a potentially better and improved nationwide strategy for the management of hypertension, which has thus narrowed the prevalence gap. To the best of our knowledge, there is yet a comparable projected estimate for hypertension cases and prevalence in Nigeria. However, research findings have shown that the prevalence of hypertension in Nigeria gradually increased from about 8.9% in the 1980s, to 15.0% in the 1990s, and increased considerably to about 22.5% in 2000 [21].

Although we aimed to provide an evidence-based, data-driven and close population representative estimates of the prevalence and cases of hypertension in Nigeria, we could have been constrained by some factors. We acknowledged there could be uncertainties surrounding our estimates, as variations in population structures, diagnostic criteria, blood pressure-measuring protocols, and effects of other health determinants (beyond age of patients) are important factors that need be considered. In addition, even with the increased output of population-based studies on hypertension in Nigeria, the number of studies retained was still relatively low, and despite an overall sample size of 27 122, study sites do not strictly spread evenly across the six geopolitical zones in Nigeria, with many of these studies conducted in the southern part of the country. Furthermore, due to lack of data, we could not provide estimates of the prevalence rates of hypertension according to the JNC classifications, particularly on pre-hypertension or borderline hypertension. One important limitation of this study was our inability to estimate the treatment and control rates of hypertension in Nigeria, which was also due to lack of

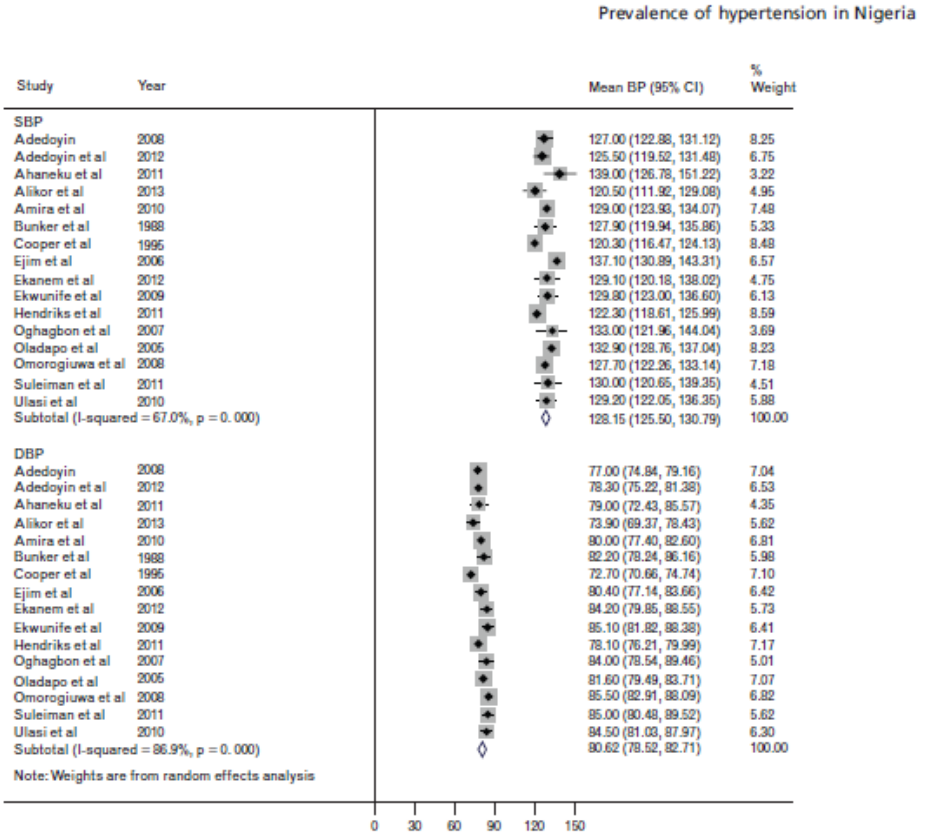

FIGURE 5 Forest plot of mean SBP and DBP in Nigeria.

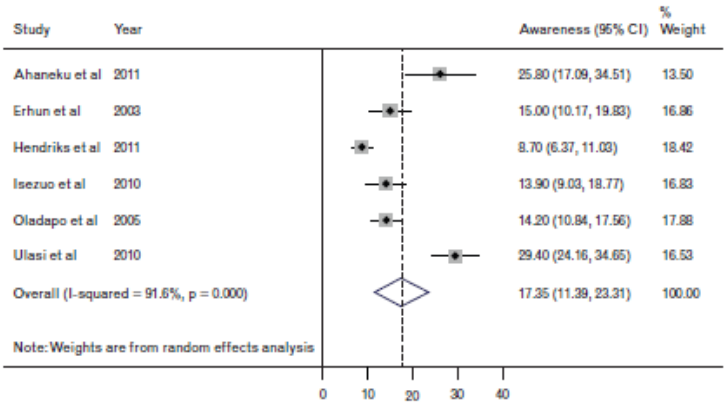

FIGURE 6 Forest plot of awareness rate of hypertension in Nigeria (expressed as percentage of overall cases of hypertension).

TABLE 5. Estimated hypertension prevalence rates and number of cases in Nigeria for 2010

Age (years)	Both sexes			Men			Women		
	Prevalence (%)	Nigerian population (000)	Hypertension cases[a] (000)	Prevalence (%)	Nigerian population (000)	Hypertension cases (000)	Prevalence (%)	Nigerian population (000)	Hypertension cases (000)
20–24	25.8	14535	3749	24.2	7393	1944	17.1	7142	1329
25–29	26.4	12643	3340	25.3	6424	1768	18.6	6219	1256
30–34	27.1	10517	2846	26.5	5358	1543	20.1	5159	1130
35–39	27.7	8237	2283	27.7	4221	1272	21.9	4017	955
40–44	28.4	6400	1817	29.0	3248	1025	23.7	3152	813
45–49	29.1	5345	1554	30.4	2656	877	25.7	2689	752
50–54	29.8	4487	1336	31.8	2183	754	27.9	2304	699
55–59	30.5	3690	1126	33.3	1764	638	30.3	1926	634
60–64	31.3	2976	930	34.8	1433	542	32.9	1543	551
65–69	32.0	2309	739	36.4	1104	437	35.6	1205	467
70–74	32.8	1566	513	38.1	733	304	38.7	832	350
75–80	33.6	909	305	39.9	414	180	42.0	495	226
80+	35.2	598	211	43.7	256	122	49.4	343	184
Total 20+	28.0 (24.6, 31.9)[b]	74213	20750	30.7 (24.9, 33.7)	37187	11406	25.2 (22.7, 31.9)	37026	9346

[a]Estimates derived from epidemiological model and based on UN population demographics.
[b]95% CI.

data. This could have been an important indicator of the response to hypertension in Nigeria. We, however, believe an estimate of the awareness rate of hypertension in Nigeria, which we provided, may relatively reflect the response to this growing burden of hypertension in the country. Finally, across retained studies, data on age and sex-specific prevalence, including corresponding data on mixed, urban and rural settings, which are vital comparative indices in any study, were not always provided (see Table 3 for overall study characteristics).

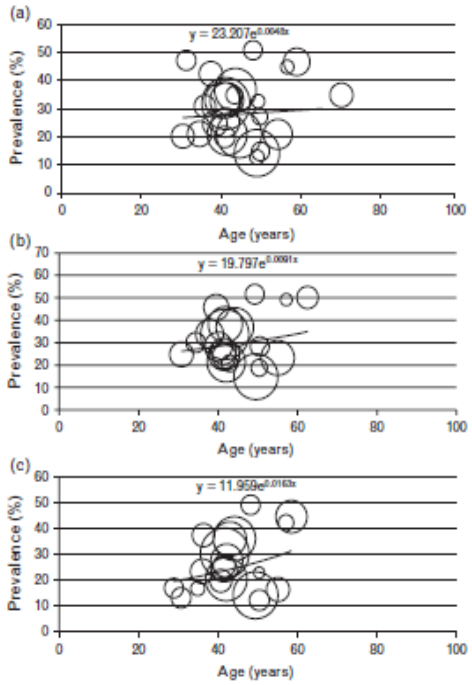

FIGURE 7 Epidemiological model showing relationship between age and crude prevalence of hypertension in Nigeria in 2010, with size of bubble corresponding to sample size. (a) Both sexes; (b) men; (c) women.

Public health response to hypertension in Nigeria

As of 2013, Nigeria still does not have a comprehensive policy for NCDs [73]. The recent communique of the National Health Council held in August 2013 points to an approval of this policy [74], yet there are still doubts on when this may be implemented. At health service delivery level, Nigeria invariably still lacks nationwide health services coverage for the awareness, diagnosis, control and treatment of hypertension [21]. In many health centres, blood pressure measurements and drug prescriptions for hypertension are not in line with the standard protocols, with poor adherence to medications often reported following complicated prescriptions [8]. The lack of standard health services has translated into poor record keeping and lack of reliable data and statistics needed to make essential health decisions on hypertension [24]. Many researchers find it difficult assessing data on hypertension and many related health issues in Nigeria, with this also leading to poor quality of research in the country [24,75].

Reports show that consumption of dietary salt is generally high in the country [9,76], and due to busy working schedules, people now consume more processed foods, and often prefer to eat from fast food restaurants [9]. Population strategies aimed at reducing salts and fats consumption and encouraging better consumption of fruits and vegetables have been shown to be very cost-effective (WHO) [77]. Experts have called for a countrywide adaptation of the Dietary Approach to Stop Hypertension (DASH) promoted by the United States National Heart, Lung and Blood Institute, as this has better dietary plans

TABLE 6. Projected hypertension prevalence rates and number cases in Nigeria for 2030

	Both sexes			Men			Women		
Age (years)	Prevalence (%)	Nigerian population (000)	Hypertension cases[b] (000)	Prevalence (%)	Nigerian population (000)	Hypertension cases (000)	Prevalence (%)	Nigerian population (000)	Hypertension cases (000)
20–24	27.7	25208	6983	25.0	12667	3163	21.2	12251	2598
25–29	28.8	20922	6017	27.0	10562	2848	23.1	10184	2353
30–34	29.9	17163	5124	29.1	8687	2530	25.2	8366	2105
35–39	31.0	14284	4428	31.5	7235	2276	27.4	6975	1912
40–44	32.2	12252	3943	34.0	6176	2098	29.9	5997	1791
45–49	33.4	10520	3515	36.7	5246	1925	32.5	5173	1682
50–54	34.7	8629	2993	39.6	4227	1675	35.4	4280	1516
55–59	36.0	6699	2413	42.8	3204	1371	38.6	3361	1297
60–64	37.4	4965	1856	46.2	2300	1063	42.0	2530	1063
65–69	38.8	3586	1392	49.9	1605	801	45.8	1851	847
70–74	40.3	2311	931	53.9	991	534	49.9	1209	603
75–80	41.8	1215	508	58.2	492	286	54.3	648	352
80+	45.1	622	281	67.9	236	160	64.4	335	216
Total 20+	30.8 (24.5–33.7)[a]	126788	39066	32.6 (27.3–38.2)	63628	20731	29.0 (21.9–32.2)	63160	18335

[a]95% CI.
[b]Estimates derived from epidemiological model and based on United Nations population demographics.

rich in fruits and vegetables, whole grains and low-fat dairy products [73]. Furthermore, tobacco industry is thriving in Nigeria and is a known factor for resistant hypertension [78]. Recently, the National Tobacco Control Bill was passed to the Nigerian National Assembly, with experts calling for strict legislations on tobacco products, including increased taxation and ban on public smoking [79,80]. Apart from the Lagos State, which recently banned smoking in public places, this generally has been difficult to implement in other parts of Nigeria, possibly due to the influence of tobacco companies on the Nigerian economy [79,81].

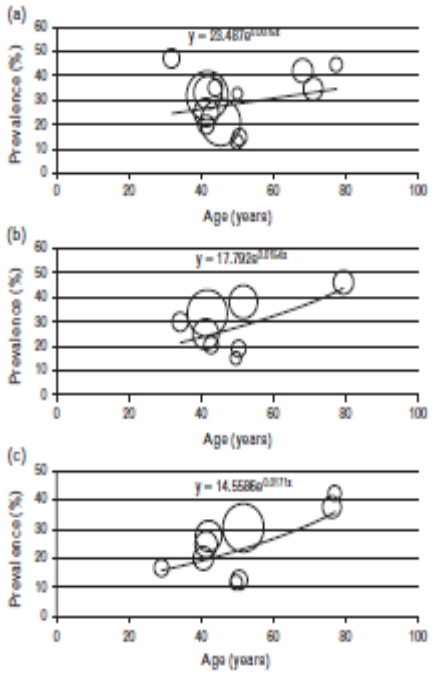

FIGURE 8 Epidemiological model showing relationship between age and crude prevalence of hypertension in Nigeria in 2030, with size of bubble corresponding to sample size. (a) Both sexes; (b) men; (c) women.

In conclusion, our findings suggest a high prevalence and low awareness of hypertension in Nigeria. With heterogeneities from various study methods and protocols, coupled with poor data record keeping, we still cannot say with certainty the exact prevalence of hypertension in Nigeria. Hypertension remains a modifiable cardiovascular risk, meaning that with adequate public health response and countrywide intervention, the burden can be reduced. There is a need for more research on hypertension and risk factors (especially from the Northern parts of the country), proper health record keeping at all levels, update of available data at national levels, all towards ensuring an improved policy response to the awareness, control, treatment and overall management of hypertension in Nigeria.

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Ethical approval: Not required.

Authorship declaration: All co-authors designed and conducted the study and contributed to the writing of the paper.

Conflicts of interest

FAO is a health systems and policy consultant to the Health Reform Foundation of Nigeria (HERFON). For the remaining authors, no conflicts of interest are declared.

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Reviewers' Summary Evaluations

Reviewer 1

Based on 27 rigorously selected studies performed after 1980, and using the current definition of hypertension, the authors estimated that 28% of the adult Nigerian population has hypertension, with slightly higher prevalence among urban than rural dwellers. Unfortunately information on antihypertensive treatment and BP control was lacking in most of the selected studies, but their prevalence can be assumed to be low in view of the mere 17% awareness rate of hypertension. The authors envisage an increase of the prevalence of hypertension to 31% in 2030, but this is only based on demographics and does not consider the potential influence of hopefully preventive lifestyle changes.

Reviewer 3

The paper by Adeloye and coworkers provides, through the use of a meta-analytic approach, comprehensive information on the epidemiological profile of hypertension in Nigeria. Strengths of the paper are its rigorous meta-analytic approach as well as the clear data discussion. Intrinsic limitations refer to the discrepancy between the different studies meta-analyzed, the methods used to assess blood pressure and the lack of data on prehypertension.