Newborn Screening for Sickle Cell Disease (SCD) in Nigeria: Factors influencing policy decisions and implementation

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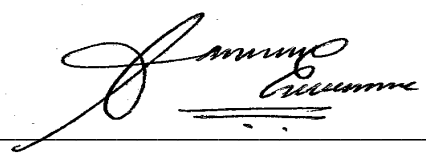
A thesis submitted in partial fulfilment of the requirement for the degree of Masters of Public Health (MPH)

By
Enwerem Kenneth Emeka
Nigeria

Declaration:
I, Enwerem Kenneth Emeka do hereby declare that this thesis "Newborn Screening for Sickle Cell Disease in Nigeria: Issues for policy decisions and implementation" is my original work. Where the work of other persons have been used from whatever source, that has been duly acknowledged and referenced in accordance with institutional requirements and international standard practices.

Signed: 

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Finally I give all the glory to God who was with me at every step of this journey. He was and always is a present help in all my times of need.

Dedication

This thesis is dedicated to every child who has lost his/her life to sickle cell disease and all children living with the disease across the globe.

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Abbreviations

ANC – Antenatal Clinic

CBOs – Community-Based Organizations

DALYs - Disability Life Adjusted Years

DPT – Diphtheria, Pertusis & Tetanus

EDL - Essential Drug List

FBOs – Faith-Based Organizations

FMOH – Federal Ministry of Health

GBD – Global Burden of Disease

GDP – Gross Domestic Product

HMIS – Health Management Information System

HPLC - High plasma liquid chromatography

JMDI – Joint Migration and Development Initiative

LGA – Local Government Area

NBS – Newborn Screening

NCDs – Non-Communicable Diseases

NDHS – National Demographic Health Survey

NPHCDA - National Primary Health Care Development Agency

PKU – Phenylketonuria

PRB - Population Reference Bureau

SCD – Sickle Cell Disease

SCFN – Sickle Cell Foundation of Nigeria

UK – United Kingdom

US – United States

WHO – World Health Organization

Abstract

Background: Newborn screening (NBS) for sickle cell disease (SCD) feasible and effective in high income countries. Introducing such programme in Nigeria (which has the highest burden of the disease) has huge potential benefits. Analysis of factors influencing its introduction is therefore crucial to ensure a successful outcome.

Objective: To explore the factors influencing the introduction and/or expansion of NBS for SCD in Nigeria.

Method: The model by Andermann et al[2010] on multiple influences on genetic screening policy decisions was adapted and used as a guide for the literature review.

Findings: Although some favourable health policies exist, the pitfalls within Nigeria's health system can hamper the implementation of NBS. SCD fulfils the classical screening criteria. Although patient advocacy groups do exert a strong influence that favours introduction of NBS, government commitment is required for sustaining the programme.
Ethical issues and cost-effectiveness are strong determinants in choice of screening methods i.e. universal or selective, mandatory or voluntary. Cost-effectiveness supports selective screening whereas universal screening is more equitable. Parental autonomy is guaranteed by voluntary participation whereas mandatory screening violates rights to justice, privacy and confidentiality but ensures protection of child's benefits against parental refusal of screening. Cultural and religious values do influence introduction of NBS.

Conclusion and Recommendations: NBS can be implemented in Nigeria however it should be integrated into existing healthcare programme. Key stakeholders should be educated and should be involved at all stages of the programme in order to influence cultural, religious and ethical values in favour of NBS.

Keywords: Newborn screening, Sickle cell disease, Nigeria, Screening criteria, Screening programmes

Word Count: 12,231

Newborn Screening for Sickle Cell Disease (SCD) in Nigeria: Factors influencing policy decisions and implementation.

Introduction

The author is a public health physician from Nigeria who has in the past three years been involved in global health advocacy for sickle cell disease as well as caring for children born with the disease under the platform of an indigenous non-governmental organization called Omega-Cares Foundation based in Jos, Nigeria. His quest for an improved quality of life for children born with sickle cell disease (SCD) has prompted the research into this topic.

This thesis examines factors that influence policy decision making and implementation of newborn screening programmes with reference to SCD in Nigeria. Newborn screening (NBS) for SCD when accompanied by comprehensive care and parental education markedly reduces morbidity and mortality associated with the disease during infancy and childhood[Nussbaum RL, Powell C, et al, 1984;Vichinsky E, Hurt D, et al, 1988; Griffiths PD, Mann JR, et al, 1988; Lees CM, Davies S, et al, 2000]. The introduction and/or expansion of such programmes are saddled with multi-factorial influences such as benefit versus risk, socio-cultural values, ethico-legal matters[Zimmmern R, Cook C,2000], human and material resources, and health system preparedness[Morgan S, Hurley J, et al 2003]. If not addressed systematically these factors may hamper and/or ultimately jeopardize the overall aim of the screening program. Other related issues include the utility of screening for additional conditions, the acceptability and feasibility of such programmes as well as equity in access to screening [National Acad. Of Sciences, 1975].

Newborn screening programmes are public health strategies which offer population-based benefits via the screening of whole or sub-set of newborns in any given population in order to offer early intervention aimed at preventing or treating disease before its apparent clinical manifestation[Last 2001]. Sickle cell disease is the most common genetic disorder globally as well as in Nigeria[World Health Organization 2006]. Substantial public health rewards can be achieved from a carefully planned and thoughtfully executed programme while minimizing the adverse effects that can result from such venture.

The growth of human genetics and genomics outpaces the application of new discoveries into public health services and often times the desire for financial gains coupled with additional pressures from advocacy, research and consumer groups often lead to a market-driven approach to newborn screening policy making[Andermann et al 2011]. This has led to difficult screening decision policies being made in the face of limited evidence of clear net benefits and lack of general consensus[Andermann et al 2011]. It is therefore crucial to holistically examine the multiple factors influencing NBS programmes and articulate the relevance of using an evidence-informed guideline in guiding decision making and implementation of such programme within the Nigerian context.

Chapter 1: Background

This chapter briefly outlines the socio-demography, ethnic composition, economy, health system and health status indices of Nigeria. It also gives a background of sickle cell disease and newborn screening in Nigeria.

1.1 Socio-demography: Nigeria is a federation of 36 states plus the federal capital territory of Abuja. According to the 2006 Population and Housing Census Nigeria has a population of 140.4 million people and an annual growth rate of 3.2%. It holds approximately one-sixth of Africa's population and is the most populous country on the continent[NDHS 2008]. Its population is expected to rise to 200 million by the year 2025. Urbanization in Nigeria is occurring rapidly, with the percentage of the population living in urban areas expected to rise from 51% to 55.4% by 2015. The country's population is relatively young: the median age is 18.7 years and about 45% of the population is under the age of 15[Population Reference Bureau (PRB) 2012].

1.2 Ethnic composition: The country is very diverse with more than 250 ethnic groups, 500 indigenous languages, and diverse religions including Islam, Christianity, and traditional African beliefs. The northern part of the country is predominantly Muslim, while the south is predominately Christian. The country has three major ethno-cultural spheres: Hausa in the north, Yoruba in the southwest and Ibo in the southeast.

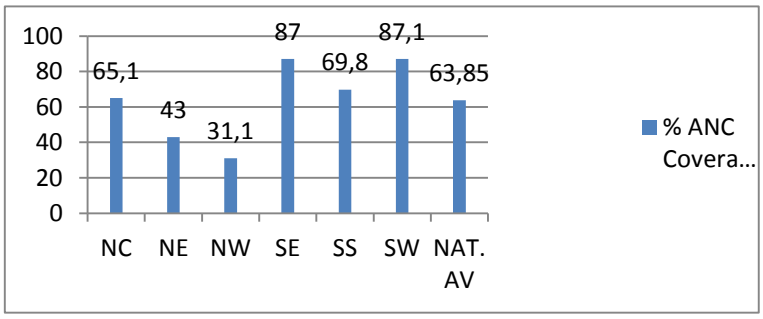
Figure 1: Map of Nigeria

Source: Federal Ministry of Health 2009

1.3 Economy: According to the World Bank, Nigeria's annual economic growth rate from 2000 through 2006 averaged 2.5% per annum. The economy is mainly dependent on huge wealth of fossil reserves, which accounts for 99% of export revenues, 85% of the government budget revenue, and 52% of gross domestic product (GDP). Agriculture, mining, telecommunication industry, and banking sectors also contribute significantly to GDP. Despite the large revenues generated from oil wealth and natural resources, Nigeria is one of the poorest countries in the world. With a GDP per capita of only about US$1,161 approximately 65% of the population lives on less than one dollar per day[World Bank 2008]. Moreover, inequalities have widened across income groups and between rural and urban areas in recent years[Oyekale et al 2006].

1.4 Health: Nigeria fares worse than similar sub-Sahara African countries on most core health indicators. According to the 2008 NDHS, 62% of births occur at home; home births being more common in rural areas (73%) than urban areas (36%). Antenatal care (ANC) coverage was 64% in 2008[figure 2]. Figure 3 shows that about 59% of children 12-23months received their first Diphtheria, Pertusis & Tetanus (DPT1) vaccinations while only 27% received all recommended immunization[NDHS 2008]. Gross regional variations exist, with the North East and North West regions worst hit due to religious based restrictions. Maternal mortality ratio of 545 per 100,000 live births is one of the highest in the world. Similarly, neonatal mortality is 39 per 1000 live births, infant mortality is 75 per 1000 live births and under-five mortality is 157 per 1,000 live births[NDHS 2008]. Malaria, HIV/AIDS, Lower Respiratory Tract Infections, Neonatal Sepsis and Diarrhoeal Disease are the leading causes of premature deaths in the country[Global Burden of Disease(GBD) 2010]. Live expectancy at birth is 48years and 54years for males and females respectively[PRB 2013]. Like other developing countries, Nigeria is undergoing the epidemiologic transition from the burden of communicable to that of non-communicable leading to the pattern now termed "the double burden of disease"[GBD 2010].

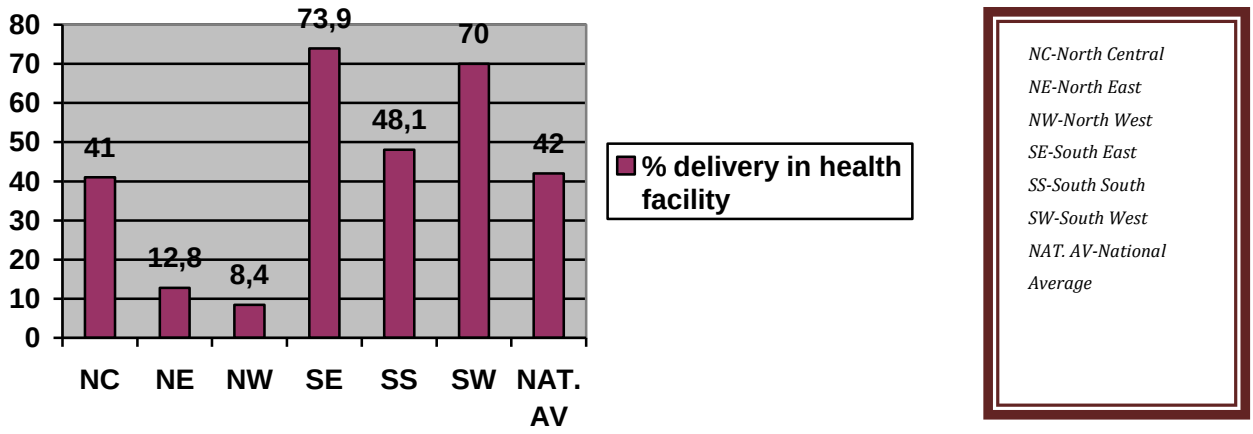
Figure 2: Antenatal coverage by geo-political zone 2008



NC-North Central
NE-North East
NW-North West
SE-South East
SS-South South
SW-South West
NAT. AV-National Average

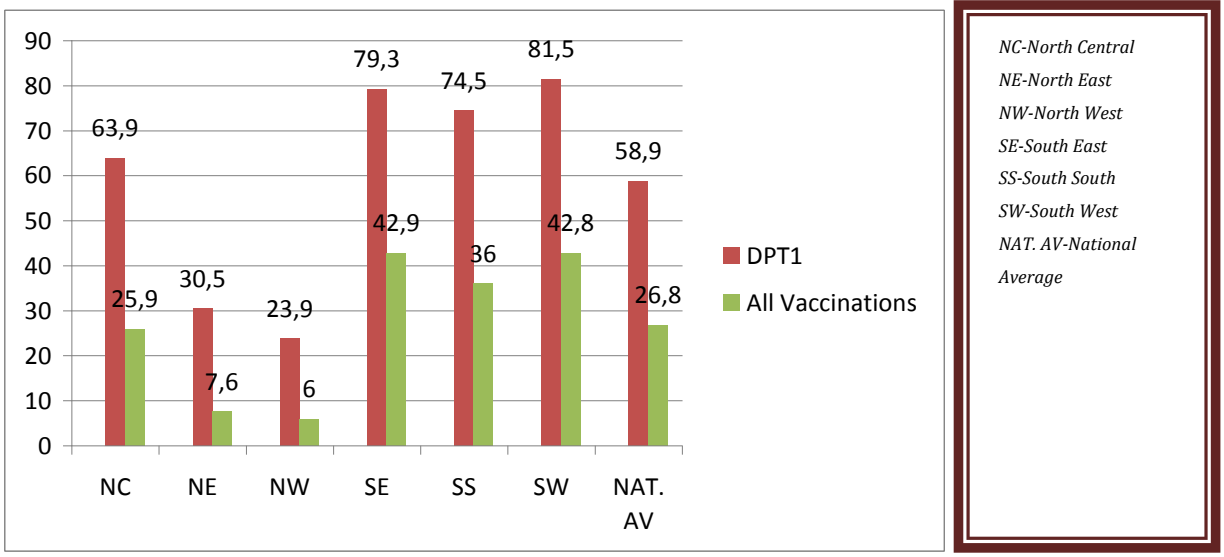
Source: NDHS 2008

Figure 3: Health facility delivery by geo-political zone 2008



Source: NDHS 2008

Figure 4: Immunization coverage by geo-political zone 2008



Source: NDHS 2008

1.5 Health System: The Nigerian health sector comprises of public, private for-profit, non-governmental organizations [NGOs], community-based organizations [CBOs], faith-based organizations [FBOs], and traditional health care providers. The health sector is very heterogeneous, and includes unregistered and registered providers ranging from traditional birth attendants and individual medicine sellers to sophisticated hospitals. According to the Department of Health Planning, Research and Statistics of the Federal Ministry of Health (FMOH), there were over 20,000 registered health facilities in the public sector in Nigeria in 2007. Private facilities constitute a third of primary care facilities and are crucial channels for partnership in the coverage expansion of key health services. The Nigerian government expenditure on health as a percentage of total government expenditure fell from 9.2% in 2007 to 5.6% in 2013[WHO

2013a] continuously failing to meet the 2001 Abuja Declaration of at least 15%[WHO 2011]. Health expenditure in Nigeria is mostly on curative services (74% of the total health expenditure), almost to the total neglect of preventive and other services which are potentially cost-saving.
Sickle cell disease poses financial burden to care-givers of affected individuals[Ohaeri & Shokunbi 2002]. Given that households continue to be the major source of health financing in Nigeria (74% of the total health expenditure in the country)[Soyibo et al 2009], healthcare services for SCD can lead to catastrophic expenditure.

1.5.1 Public Health Sector: The Nigerian federation is in principle decentralized into a three-tier structure with responsibilities at the federal, state and local government levels.

1.5.1a Federal Government: The federal government via the FMOH is responsible for policy development and guidance, planning and technical assistance, coordinating implementation of the National Health Policy, management of the national health information system and provision of health services via the tertiary facilities. These facilities have special expertise and technological capacity that enable them to serve as referral centers for patients from lower levels of care and act as resource centers for knowledge generation and diffusion. Each state has at least one tertiary facility[FMOH 2009].

1.5.1b State Government: State governments via the State Ministries of Health and State Hospital Management Boards manage secondary level of care. They provide technical assistance to local government health programs and facilities. Secondary care facilities provide general medical and laboratory services as well as specialized health services and serve as referral centers for primary care facilities. They are typically staffed by physicians, nurses, midwives, laboratory and pharmacy specialists, and community health officers (CHOs). Each district, local government area (LGA), or zone has at least one secondary-level facility[FMOH 2009].

1.5.1c Local Government: LGAs manage primary health care. Facilities at this level form communities' entry point into the health care system. They include health centers, ward clinics and dispensaries, and health posts which typically provide general preventive, curative, promotive, and pre-referral care. Table 1 shows that non-communicable disease (including SCD) prevention is a component of the ward minimum health care package (WMHCP) in Nigeria[National Primary Health Care Development Agency (NPHCDA) 2007].Primary facilities are typically staffed by nurses, CHOs, community health extension workers (CHEWs), junior CHEWs, and environmental health officers.

The coverage of most key preventive and curative health services in terms of number of services offered, number of people reached and financial coverage is relatively low in Nigeria. This is further compounded by the disparities that exist along socio-economic, rural-urban and geo-political divides[FMOH 2009].

Table 1: Ward Minimum Health Care Package

1	Control of communicable diseases(Malaria, STI/HIV/AIDS,TB)
2	Child Survival
3	Maternal and newborn care
4	Nutrition
5	Non-Communicable Disease Prevention
6	Health promotion and community mobilization

Source: National Primary Health Care Development Agency 2007

1.5.2 Private Health Sector: The private sector is a key stakeholder in the provision of healthcare across the country. Its wide range of coverage which includes hard-to-reach rural areas gives it an advantage over the public sector. It has a wide range of providers including physician practices, maternity homes, clinics, and hospitals. Private for-profit health facilities have proliferated since the mid- 1980s and together with FBOs, provide 80% of health services[Larbi et al 2004].
Private for-profit facilities provide mostly curative services, while the FBOs provide a wider range of preventive and health promotion services. There are also traditional medicine practitioners and informal medicine vendors. While the private sector makes an appreciable contribution to health care in Nigeria, the sector is not very well regulated and supported owing to weak policies, guidelines, and manuals[FMOH 2009].

1.6 Sickle Cell Disease: Global and Nigerian perspective

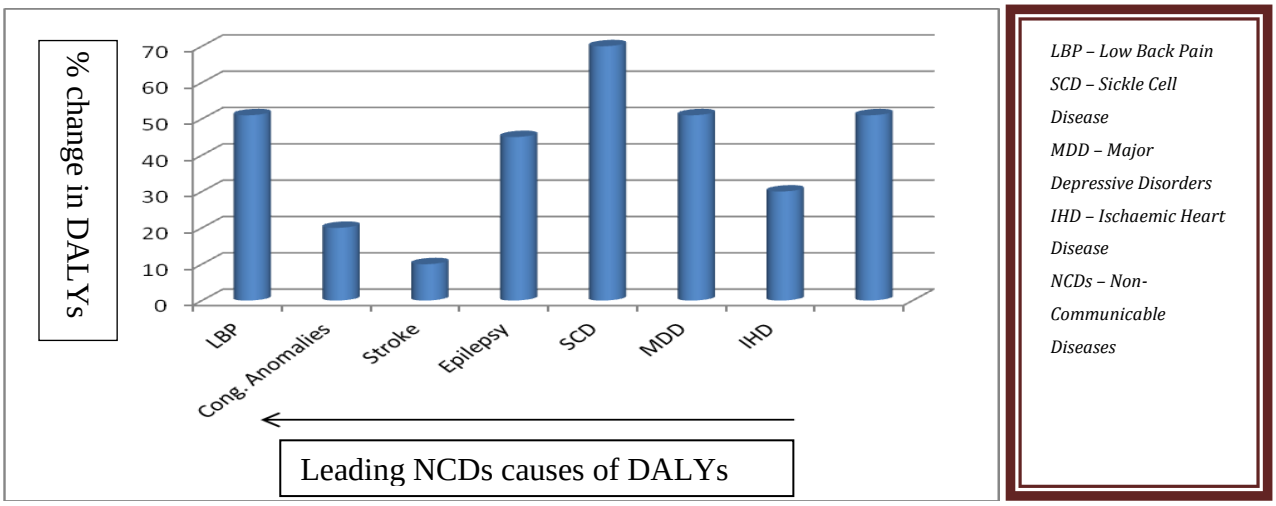
Sickle cell disease represents a group of related lifelong inherited genetic blood disorders of haemoglobin characterized by repeated episodes of bone pain crises, chronic anaemia and multi-organ damage with an increased risk of early death. Sickle cell anaemia [HbSS] is the most severe form of the disease. Other less severe forms include HbSC and HbSBthal[Quinn et al 2010]. Sickle cell disease was discovered in 1910 by a Chicago cardiologist, Dr James Herrick.[Herrick 1910] Its origin has been traced to a mutation in the haemoglobin component of red blood cells owing to the human body's effort at protecting itself from malaria parasite. Therefore individuals who carry a single sickle cell gene – sickle cell trait (HbAS) are better protected from malaria than those who do not[Ferreira et al 2011]. This explains the similarity in global distribution for both SCD and malaria[Allison & Phil 1954].

Between 5% and 7% of the world's population are healthy carriers[HbAS] of the sickle cell gene, and over three hundred thousand (300,000) children are born with the disorder every year, making SCD the most common inherited blood disorder in the world[Weatherall & Clegg 2001; Weatherall 2006; Weatherall et al 2006]. Amidst a high prevalence and high mortality attributed to the disease[Leikin et al 1989; Platt et al 1994; Weatherall et al 2006], the WHO only recently recognized SCD as a major public health problem and declared it a public health priority[WHO 2006].

Sickle cell disease has been identified as one of the top ten non-communicable diseases in the Nigeria and contributed the highest

percentage change in disability life adjusted years (DALYs) between 1990 and 2010 attributable to non-communicable diseases (NCDs) in Nigeria as shown in figure 5[GBD 2010].

Figure 5: Non Communicable Diseases: Leading causes of DALYs and percent change 1990 to 2010 for Nigeria



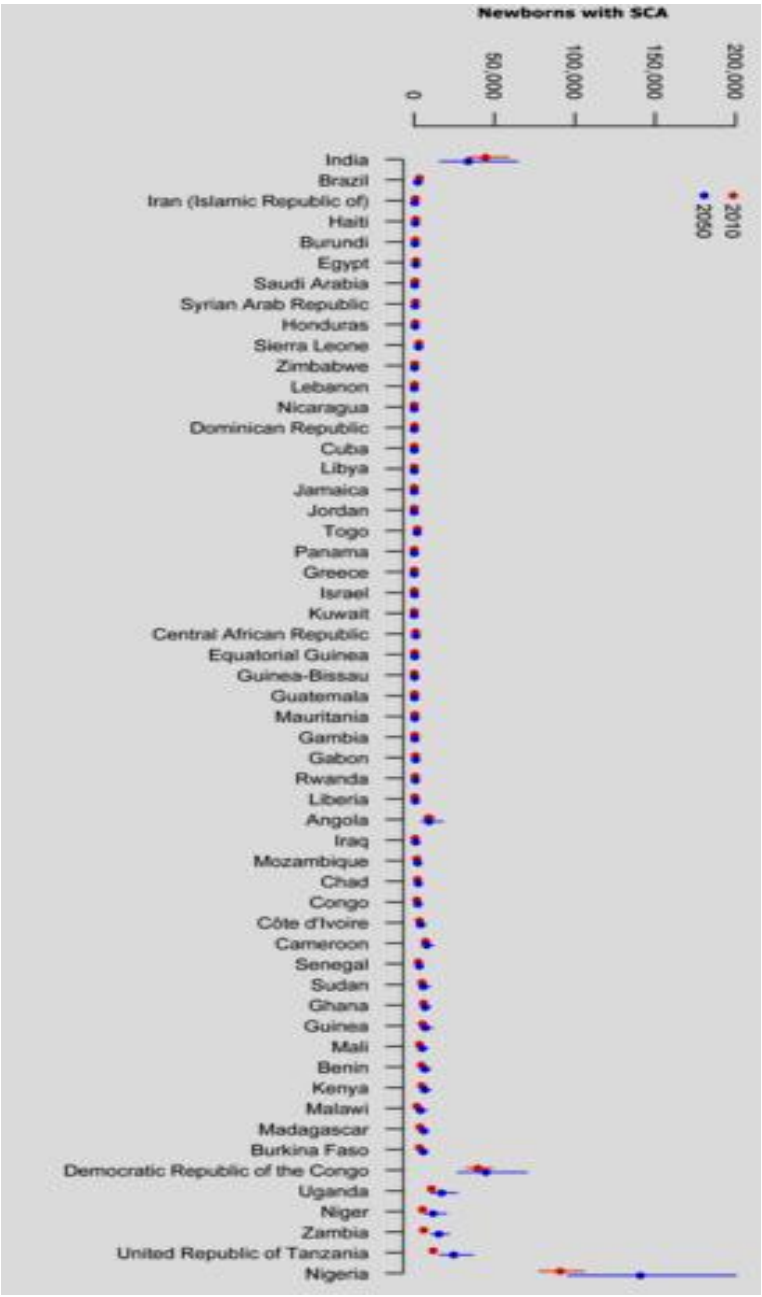
Source: [Adapted from GBD 2010]

Though the prevalence of the disease is relatively similar (2-3%) across equatorial Africa[Tshilolo et al 2008; Grosse et al 2011] Nigeria accounts for about half of the total global burden of SCD[WHO 2006] on account of its huge population. Twenty-five percent of Nigerians(about 35million people) are healthy carriers of the sickle cell gene and 20 out of every 1000 children are born with the disease anually; resulting in 150,000 SCD births per year[Akinyanju 2009]. These figures were based on a 1972 survey in Nigeria and their current validity is questionable. Recently published modelling estimates[figure 6] however put this figure at 91,000 for 2010 and a projected 140,800 by 2050[Piel et al 2013].

The World Health Organization (WHO) estimates that 70% of deaths from SCD in Africa are preventable with simple, cost-effective interventions such as early identification of SCD patients through NBS and subsequent provision of comprehensive care. The WHO therefore recommends a well-structured coordination of all activities geared toward SCD prevention, management and control[WHO 2006]. Efforts have begun with the establishment of the Sickle Cell Foundation of Nigeria (SCFN) in 1994 led by Professor Olu Akinyaju-[Akinyanju 2009] to address the problem of SCD in a systematic, scientific and sustainable manner. The foundation has set up the National Sickle Cell Centre in Lagos Nigeria as a national coordination body which oversees the activities of state units and each state unit will in turn supervise and coordinate the programmes and activities of all sickle cell clubs within the state. The Nigerian Sickle Cell Expert Advisory Committee has also been constituted to consider, initiate and revise policies and strategies appropriate to the management, prevention and control of SCD in Nigeria. According to the SCD desk officer at the FMOH, Dr S. Alayo, the Nigerian government has established

six special SCD centers across the six geo-political zones of the country which will be used for pilot NBS in each zone.

Figure 6: Country ranking based on estimated number of newborns with SCA in 2010 and 2050.



Source: [Piel et al 2013]

1.7 Newborn Screening Programme

Newborn screening is a public health initiative that surveys all newborns in an entire population (or sub-population) for evidence of an illness before it exhibits symptoms with the aim of identifying those among the apparently well who are suffering from (or will likely develop) a disease and who are likely to benefit from early detection and intervention[President's Council on Bioethics 2008]. Newborn screening

usually begins with a blood test 24 to 48 hours after the baby is born. The test is performed by pricking the baby's heel to collect a few drops of blood. The blood is placed on a special piece of paper and sent to a laboratory for analysis. Newborn screening goes beyond just a laboratory test. It is a system that comprises of six essential components[President's Council on Bioethics 2008]:Education, Screening, Early follow-up, Diagnosis, Management, and Evaluation (table 2).

Table 2: Components of a Newborn Screening Programme

No	Component	Description
1	Education	for health professionals, parents, general public and policy makers
2	Screening	proper timing and specimen collection, transport, laboratory testing and reporting.
3	Early follow-up	notification of results, tracking of affected infants and confirmatory testing
4	Diagnosis	clinical and biological evaluation
5	Management	counselling, treatment, monitoring and long term follow-up
6	Evaluation	monitoring of outcome and quality assurance throughout the system

Source: President's Council on Bioethics 2008

1.8 Pilot Newborn Screening Programme in Nigeria

According to Dr Baba Inusa, the initiator of the program, a pilot NBS for SCD in Nigeria was initiated in 2009 and funded by the Joint Migration and Development Initiative[JMDI] – a United Kingdom (UK) based organization. It was a hospital-based program in Zankli Medical Center [ZMC] in the nation's capital city. A universal, but voluntary screening approach was adopted. Pregnant women attending ANC in the host facility were given pre- and post-natal education and counselling about the screening and their children were tested (using the High Plasma Liquid Chromatography [HPLC] machine) immediately after birth after informed consent had been obtained verbally. The mothers could opt-out of the screening without any repercussions. Affected children were then enrolled into a comprehensive care program which involved antimalarial and penicillin prophylaxis, parental education and folic acid administration. There was provision for pneumococcal vaccination to those who could afford this relatively expensive drug. The programme ended in 2011 and although an evaluation is yet to occur, it has been adopted by the host facility and pilot programmes have commenced in two states in the country (Kaduna and Katsina) both in the North-West zone. The programme in ZMC is paid for by the recipients but that in the two north-western states are government sponsored as both state governments provides free maternal and child healthcare services. As at time of submission of this thesis, I was yet to receive the manuscripts for the findings of the pilot study; however Dr Baba Inusa described it as successful. The main challenge faced was tracking the affected kids to notify parents of the results and follow-up of referred cases. A similar experience occurred in Ghana where only 20% of families returned for their results[Ohene-Frempong et al 2008]

1.9 Newborn Screening versus Pre-marital/Prenatal Screening

Although pre-marital and prenatal screening are primary prevention strategies as against secondary prevention of NBS, this thesis focused on the latter because:

(1). there are on-going pilot NBS programmes for SCD in the country and the findings in this study will contribute to better decision making as to the progression from pilot to state-wide implementation;

(2). Pre-marital and prenatal screening for SCD are marred with certain constraints which makes their selection unfavourable:

- Rights of Association: pre-marital screening usually occurs at points when couples have made their decision to get married and is usually followed by advice of discontinuation of the relationship. Couples see this as a breach of their right of association[Lisko 2008], and according to a Saudi Arabia study 89.6% of high-risk couples still went ahead with their relationships despite the known high-risk status. [Alhamdan et al 2007]
- Rights of Reproduction: prenatal screening faces ethical challenges as the option of termination of pregnancy provided after screening, violates ethical and religious values and laws in Nigeria[Ahmed et al 2006; Ilobinso 2007]

Chapter 2: Problem Statement & Justification, Objectives, Methodology

This chapter examines the problem under study, the justification for and the objectives and methodology of the study as well as the conceptual framework used to analyse the findings.

2.1 Problem Statement

Mortality from SCD has remained high. In Africa about 50-90% of children with SCD die in the first five years of life and about 50% of these deaths occur in the second six months of life[Makani et al 2011;Rees et al 2010;Serjeant 2005;Williams et al 2011]. Most cases of the disease go undiagnosed, as parents are unaware of its presence and the diagnosis is often made post-mortem[Vichinsky et al 1998]. Thirty percent of the children who died from SCD did so before their parents were aware of the presence of the disorder[Lee et al 2000; Vichinsky 1991]. In certain parts of West African region SCD accounts for nearly 20% of neonatal mortality[Modell & Darlison 2008; Makani et al 2007]. In Nigeria, SCD is the sixth leading cause of death in under-fives and deaths from infections and acute splenic sequestration crisis rank the highest among the causes of these early deaths[Child Survival, Protection and Development (CSPD) in Nigeria 1995].

Newborn screening reduces the morbidity and mortality associated with SCD in childhood[Lee et al 2000;Quinn et al 2004;Telfer et al 2007;Vichinsky et al 1998]. Yet there continue to be obstacles around policy decisions and implementation of NBS including financing, education, resource requirements, religious and cultural sensitivity, education, and political support[Therrell 2003]. All NBS programs exist within the limitations of their local environment and various examples of navigating these barriers are discussed.

There are however some risks associated with NBS. The incidental detection of sickle cell carrier status and other haemoglobin disorders of questionable clinical significance can cause psychosocial harms, which include exposure of paternity, stigma and discrimination, negative impact on self-esteem, and anxiety about future health[US Preventive Services Task Force 2008]. In an article I co-authored on the knowledge and behaviour of secondary school students in Nigeria toward SCD, sickle cell carrier status will influence the choice of life partner in more than half of students, while a third of students will end a relationship if they discover that their partner has SCD[Olarewaju et al 2013].

2.2 Justification

The burden of SCD in Africa is increasing. Due to population growth, there is a projected increase in the number of newborns with SCD to over 400,000 in 2050[GBD 2010]. However mortality rates are projected to

decline to as low as 5% in low-/middle-income countries if universal screening programme is implemented.[Piel et al 2013] At present only one country in sub-Saharan Africa (Ghana) has a functional national universal NBS programme; a scale-up which followed the success of a pilot programme launched in 1993[Ohene-Frempong et al 2008]. A couple of African countries including Angola[McGann et al 2012], Benin[Rahimy et al 2009], Burkinafaso[Tshilolo et al 2008] and Democratic Republic of Congo[Tshilolo et al 2009] have published their experience from pilot programmes on NBS for SCD; all of which showed that NBS for SCD is feasible in low-middle income countries. Although certain private initiatives for hospital-based and community-based screening exist in Nigeria[Kolawole 2012; Olusanya et al 2005; Oputa 2009], a national NBS for SCD is yet to be established. A pilot NBS for SCD was commenced in 2009[JMDI 2009] and the outcomes are yet to be evaluated.

Beyond the classical Wilson and Jungner screening criteria and principles[Wilson & Jungner 1968](appendix 3), there are a number of multiple factors which influence genetic screening policy decisions and implementation. These factors include key stakeholders' influences, ethical and social values, and contextual health system policies and frameworks. Although studies have been conducted in developed settings examining the influence of such factors on NBS[Zimmern & Cook 2000; Haddow & Palomaki 2004], none has as yet been conducted to determine the collective influence of these variables in guiding policy decisions and implementation of screening programme in a low resource setting like Nigeria. This study therefore aims to explore the influences of such factors in guiding implementation of NBS programmes.

2.3 Objectives of the thesis

2.3.1 Overall goal

This study aims to explore the factors influencing the policy decisions and implementation of newborn screening for sickle cell disease in Nigeria in order to proffer recommendations to policy makers as well as healthcare providers on appropriate strategies that will contribute to the successful implementation of such programme.

2.3.2 Specific objectives

1. To examine the suitability of SCD for NBS programme in Nigeria using the screening criteria and principles.
2. To identify and examine the health system's preparedness for NBS with respect to organizational structure and policies/guidelines.
3. To explore the influence of key stakeholders and their values/preferences in the introduction and/or expansion of NBS and the context in which these programmes exist.
4. To proffer recommendations to policy makers as well as healthcare providers on appropriate strategies for successful implementation of such programme.

2.4 Methodology: The methodology involved a literature search to identify relevant information on the topic as well as key informant interview to correlate and contextualize the data.

2.4.1 Literature Search: A preliminary search using Google Scholar search engine was done to identify literature on the topic of study. Database searches were then conducted in an iterative manner to retrieve articles related to the study subject from COCHRANE LIBRARY, PUBMED, MEDLINE, SCOPUS and Science Direct to complement as well as streamline the preliminary search. The websites of FMOH, WHO and United Nations Children Fund [UNICEF] were also searched for relevant materials. Reference lists of published articles were reviewed to find additional articles.

2.4.1a Keywords: Keywords used were "newborn screening", "neonatal screening", "screening criteria", "screening programmes", "screening policy framework and implementation", "genetic screening and ethical issues", "screening programmes and resource-low settings", "sickle cell disease", and "sickle cell disease and Nigeria", "sickle cell disease and sub-Saharan Africa" and various combinations of these.

2.4.1b Inclusion and Exclusion Criteria: The search was restricted to publications in English. Except where recent articles on the topics could not be found or articles which described framework/criteria for screening that may date back before, the searches were restricted to articles published from the year 2000 to allow for current information on the topic. The search included studies done in both resource-limited and high-income settings in order to have a fair comparison of study area with international and regional settings.

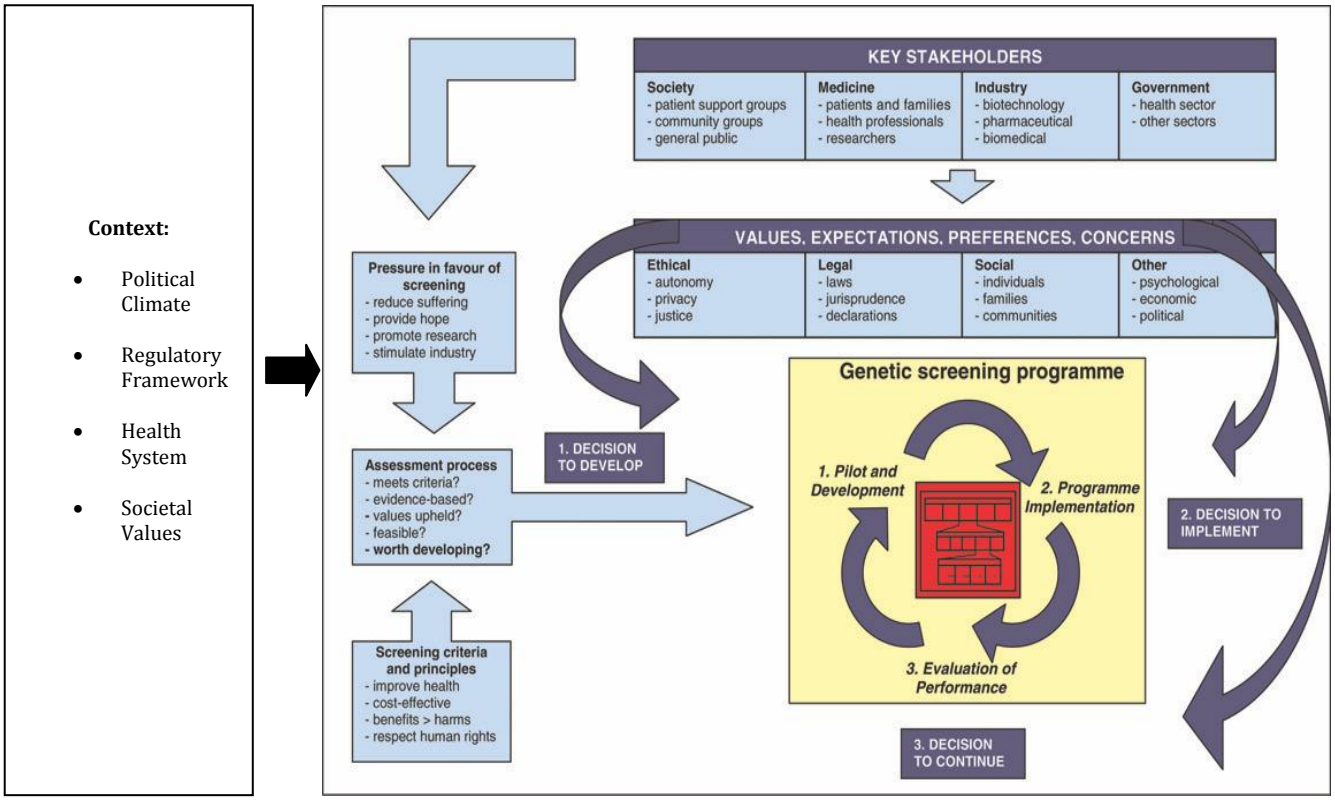
2.4.2 Key informants: Two key informants (the SCD desk officer at the FMOH & the initiator of the pilot NBS for SCD Nigeria) were interviewed via telephone communications and emails.

2.5 Conceptual Framework

The framework as depicted by figure 7 was used for the presentation, analysis and discussion of findings. The initial framework (Appendix 2) was developed by Andermann et al[2010] as part of a 3-part framework which looks at genetic screening programmes in terms of levels of operation, multiple influences on screening policy decisions and implementation and multilayered context for screening policy-making. Because the focus of this thesis is on factors influencing policy decisions and implementation of NBS as well as the contextual settings in which these decisions and implementation occur, the second and third parts of the original framework have been merged together to give the desired study framework. The framework introduces the element of screening criteria and principles as a pre-requisite for the assessment process in determining if a given disease condition should be included into a screening programme. It also elaborates the key stakeholders involved in the decision process as well as their values, expectations, preferences and

concerns and how these result in pressure on favour of screening programme. Pressure from stakeholders and screening criteria assessment lead to the primary decision to develop a genetic screening programme usually in the form of a pilot. A proper implementation of the programme ensues if the pilot succeeds and following evaluation of performance of the programme, it is either consolidated (if successful) or re-piloted with modifications or entirely scrapped off. Since the focus of this thesis is on NBS for SCD in Nigeria which is yet to be introduced on the national level (although a hospital-based pilot is currently on-going), the discussions have been limited to the various factors influencing the introduction of the NBS programme.

Figure7: Multiple influences on genetic screening policy decisions throughout the lifecycle of the programme



Source: adapted from Andermann et al 2010

2.6 Limitations

The search was limited to literature published in English. A few studies in other languages may have provided more contextual insight. It was difficult to get information from the FMOH as well as the host health facility for the pilot NBS for SCD in Nigeria. Only few articles on studies done in Nigeria or similar low resource settings on the study topic were found as NBS is a relatively new field in developing countries; most of the articles were on studies done in developed settings. A full-fledged field work would have been more informative for this study and provide a more robust contextualization of data.

CHAPTER 3: PREPAREDNESS FOR NEWBORN SCREENING: HEALTH SYSTEM AND POLICY

This chapter analyzes the preparedness of the health system toward introduction of NBS for SCD by examining its policies and resources. It also examines the context in which NBS programmes are initiated and implemented. The experiences in other countries are highlighted.

The presence of an adequate skilled human resources and facilities for diagnosis and treatment is crucial for NBS. This has evolved over time to include a comprehensive programme which integrates education, testing, clinical services and programme management[Andermann et al 2010]. Beside the regular cadre of health professionals (doctors, nurses, laboratory scientists, etc), a crucial requirement for human resources in NBS is trained genetic counsellors who play key roles in the whole process. Also crucial is the enabling policy environment for the screening programme.

3.1 Health System

A national health system assessment conducted in 2008 based on the six building blocks of the World Health Organization was used to analyse the Nigeria's health system preparedness toward the implementation of NBS programme.

3.1.1 Human Resources for Health: At figures of 30 doctors and 100 nurses per 100,000 people[Table 2] the country enjoys a relatively sound supply of human resources when compared to similar countries in the sub-Saharan region (although wide variations exist across geo-political zones within the country[Table 3]). Before NBS can commence healthcare professionals involved need adequate training. No cadre exist for the position of genetic counsellors in the human resources for health of the country[Scott-Emuakpor 2010]. The SCFN commenced training of health workers in genetic counselling in 1986. About 420 health workers have been trained thus far. An opportunity exists in the area of integrating genetic counselling for SCD and counselling for HIV testing since a robust programme and human resource already exists for the latter[WHO 2005]. Following an evaluation of its pilot NBS the Ghana Health Service trained additional 600 health workers in all its ten regions in preparation for scale-up of its NBS programme[Ghana Health Service 2011].

Table 3: Human Resource for Health in Nigeria

Staff Category	Numbers	Per 100,000
Physicians	39,210	30
Dentists	2,773	2
Nurses	124,626	100
Midwives	88,796	68
Pharmacists	12,072	11
Physiotherapists	796	0.62
Occupational Therapists	210	0.16
Medical Lab Technicians	3,059	3
Radiographers	519	0.42
Primary Care Workers	117,568	93

Source:[Scott-Emuakpor 2010]

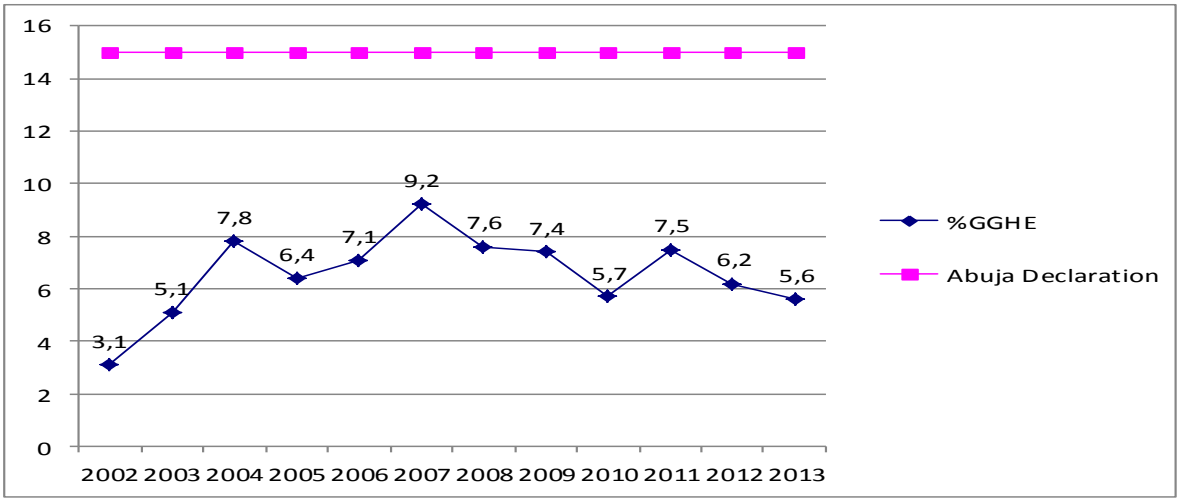
Table 4: Number of Health Professionals by Cadre and Geopolitical Zone

Zone	Doctors		Nurses and Midwives		Medical Laboratory Scientists		Pharmacists		Total	
	No	%	No	%	No	%	No	%	No	%
North East	675	4	3398	15	96	2	245	4	4414	8
North West	1388	8	3941	17	201	3	502	8	6032	10
North Central	1841	11	5778	25	434	8	1342	20	9395	16
South East	3210	20	4914	22	2110	37	841	13	11075	19
South West	7300	44	4487	20	1603	28	2859	44	16249	28
South South	2618	13	7097	31	1281	22	743	11	11289	19
Total	16582	100	22518	100	5725	100	6532	100	58454	

Source: [Adapted from FMOH 2009]

3.1.2 Health Financing: Health financing is essential to and facilitates the successful implementation of NBS. Although some improvement has been made, the Nigerian government is yet to achieve the Abuja Declaration target of committing at least 15%[figure 8] of her national budget to healthcare[WHO 2011]. Meeting this target can boost financing of NBS programmes. Partnership funding can also facilitate the implementation of NBS programmes especially in low-income settings as governments alone are unable to bear the cost. Currently the pilot program in Nigeria is receiving support from JMDI. The Brazil-Ghana partnership[Alhassan 2010] and the USA-Ghana partnership[Ohene-Frempong et al 2008] has also contributed to successful implementation of NBS programme in Ghana.

Figure 8: General Government Health Expenditure (GGHE) as a Percentage of General Government Expenditure



Source: [Adapted from WHO 2013a]

3.1.3 Service Delivery: Sickle cell disease management in Nigeria is mainly offered in secondary and tertiary facilities and even though the WMHCP includes prevention of NCDs (SCD inclusive), implementation is yet to commence[NPHCDA 2007]. Most children (62%) are delivered outside health facilities and will therefore be missed in NBS programmes. A potential for increased coverage of NBS exists in its integration into already existing government public health programmes like immunization which has a fairly good coverage (59% for DPT1 vaccination)[NDHS 2008].

3.1.4 Health Information Systems(HMIS): The national policy on NCDs reiterates the need for a comprehensive data collection on clinical and social aspects of NCDs including SCD. However the HMIS lacks adequate data on SCD in terms of epidemiology, demographics, cost and utilization pattern of services, etc. Available data are only from local researches which are few and non-representative of the entire country.

3.1.5 Pharmaceutical Management: Government has made some progress in developing national policies and guidelines for the pharmaceutical management system of SCD. The Nigeria Essential Drug List (EDL)[FMOH 2010] contains all drugs used in the treatment of SCD which are currently on the WHO recommended list[Neville & Panepinto 2011] except for hydroxyurea (conventionally used in cancer treatment) due to concerns of drug toxicity.
In 2012 the FMOH along with the National Institute for Pharmaceutical Research and Development (NIPRD) and the Nigeria Export Import Bank (NEXIM Bank) signed a Memorandum of Understanding for the production of the SCD drug - Niprisan[Editor Business News 2012]. Although this drug is not on either the EDL of WHO or Nigeria, it has shown good clinical efficacy for the management of SCD[Wambebe et al 2001].

Table 4. Drugs used in the treatment of SCD which are currently on the EDL

Class of Drugs	**Names of Drugs**
Disease Modifying Agents	hydroxycarbamide (hydroxyurea)*
Supportive Care Agents: Analgesics	Paracetamol ibuprofen codeine morphine
Supportive Care Agents: Antibiotics	phenoxymethylpenicillin cefotaxime
Supportive Care Agents: Pertinent Vaccines	pneumococcal vaccine
Supportive Care Agents: Systemic Treatments	Parenteral 5% glucose, 0.45% sodium chloride Red blood cell transfusion
Supportive Care Agents: Iron Chelators	Deferoxamine

*On list for treatment of cancer not sickle cell disease; also not on essential medicines list for Children.
Source: Neville & Panepinto 2011.

3.1.6 Governance: Recent efforts at health sector reforms are yet to yield desired outcomes. Full government commitment is a definite requirement for this. In a conversation with B. Inusa MD, (August 2013), he reiterated that the federal government and FMOH are yet to show full commitment toward the NBS programme. A comprehensive Bill for SCD management (Appendix 4) sponsored in the National Assembly by two

senators [Ifeanyi Okowa and Nenadi Usman] did not win majority vote among policy makers in 2012. Kaduna and Katsina state governments (north-west of Nigeria) have however shown commendable support for the pilot scheme in their states. In Ghana, the commitment and support (organizational, infrastructural and staff) from Ghana Ministry of Health and the Ghana Health Service contributed to the success of the NBS pilot program[Ohene-Frempong 2005].

3.2 Health Policies and Guidelines: The revised national health policy as well as other policies/guidelines which address NCDs, SCD and NBS are identified and examined in this section in order to further ascertain the readiness of the health system for NBS toward SCD.

3.2.1 Revised National Health Policy 2004 [FMOH 2004].

The overall goal of child health policy in this document is the protection of children's health and ensuring their survival, healthy growth and development. This includes the reduction of infant and under-five mortality rates.[FMOH 2004] And although SCD is said to contribute to about 8% of infant mortality and 16% of under-five mortality in the country[WHO 2006], there was no mention of strategies for tackling this burden. The policy mentioned SCD only in a phrase under section 7.6 (sources of health data and information) – where it says "disease registers for specific mortality and mortality shall be kept such as for cancer, SCD, …, etc", though this is hardly implemented. Nevertheless the policy has a target toward the commencement of NBS programmes for childhood hearing loss. Ghana's child health policy has screening for SCD as a key component of its neonatal period interventions[Ministry of Health of Ghana 2007] and this is currently being implemented.

3.2.2 National Policy on Non-Communicable Diseases (NCDs) [FMOH 2011]

The mission of this policy is "the prevention and control of NCDs risk factors, reduction in morbidity as well as mortality and promote healthy lifestyle for all in Nigeria"[FMOH 2011]. This policy recognizes the increasing contribution of NCDs to the national burden of disease due to the epidemiologic transition. Sickle cell disease is recognized as one of the top ten non-communicable diseases in the country alongside hypertension, diabetes mellitus, coronary heart disease and cancers.

Sickle cell disease was mentioned as a risk factor for stroke in children and a leading cause of stroke in childhood in Nigeria. Among the strategic thrusts and actions for policy implementation are –

- "*Screening and early detection of NCDs and their risk factors"*
- *"Integration of NCDs management into primary healthcare services and provision of framework for private sector participation"*
- *"Mandatory routine screening for sickle cell disorder (pre-marital and newborn), hypertension, diabetes, and some cancers"*.

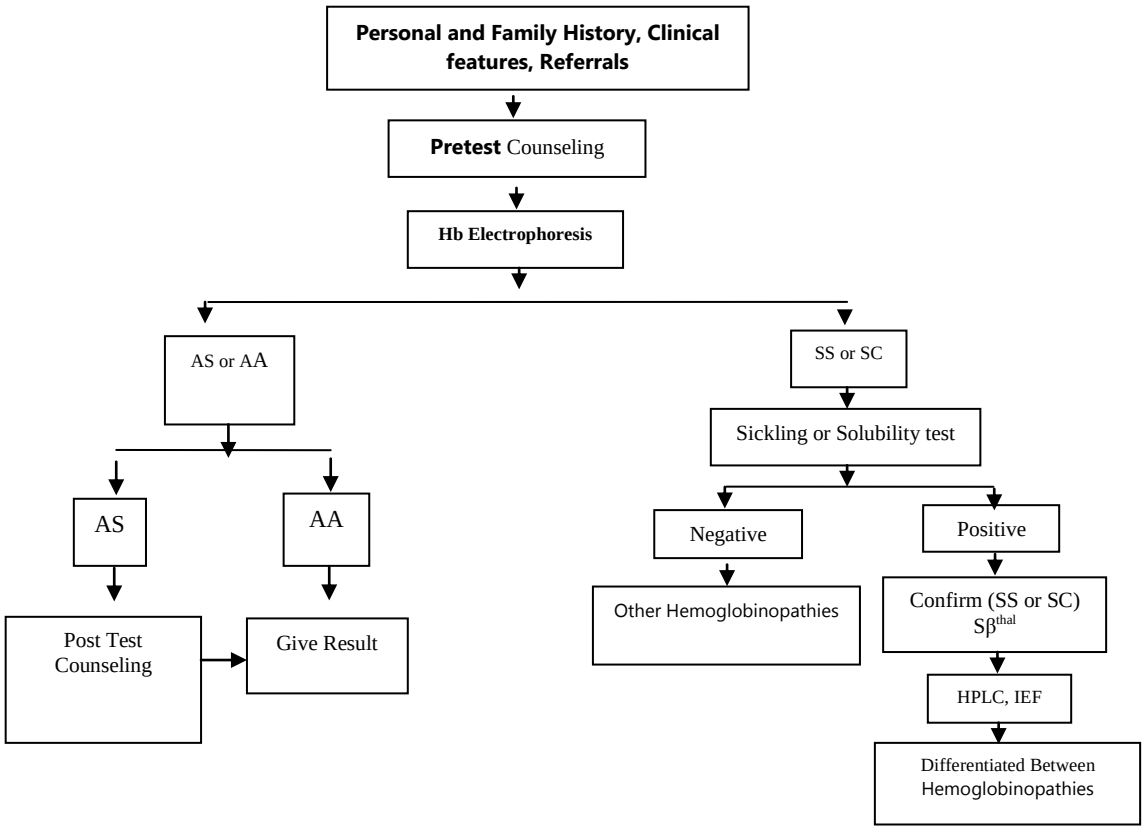
This shows a good attempt by this policy to incorporate SCD prevention and control into the NCD programme of the country. Mandatory screening may however raise ethical issues of autonomy, privacy and justice. A pre-marital screening is also not a favoured approach in the country as religious and legal regulations forbid the option of termination of pregnancy which follows such screening.

3.2.3 Nationwide Guideline for the Control and Management of Sickle Cell Disorder [FMOH 2012]

This guideline was developed to provide direction for the control and management of SCD symptoms and complications. The specific areas of the guideline which are relevant to the thesis topic of NBS are highlighted here.

3.2.3a Laboratory diagnosis: A pathway for the definitive laboratory diagnosis of SCD is created in this guideline. The diagnostic methods used here include sickling test, solubility test, haemoglobin electrophoresis and high plasma liquid chromatography (HPLC). It recommends at least two tests which must be unrelated in their method of diagnosis. Currently however only the haemoglobin electrophoresis is available in most tertiary and secondary facilities across the country[Kotila TR 2010]. The HPLC machine is only available in ZMC donated by the pilot NBS program and in Katsina state donated by the state government. Figure 9 shows an algorithm for the diagnosis of SCD.

Fig 9:Alogrithm for definitive laboratory diagnosis for sickle cell disease



Source: Nationwide Guideline for the Control and Management of Sickle Cell Disorder

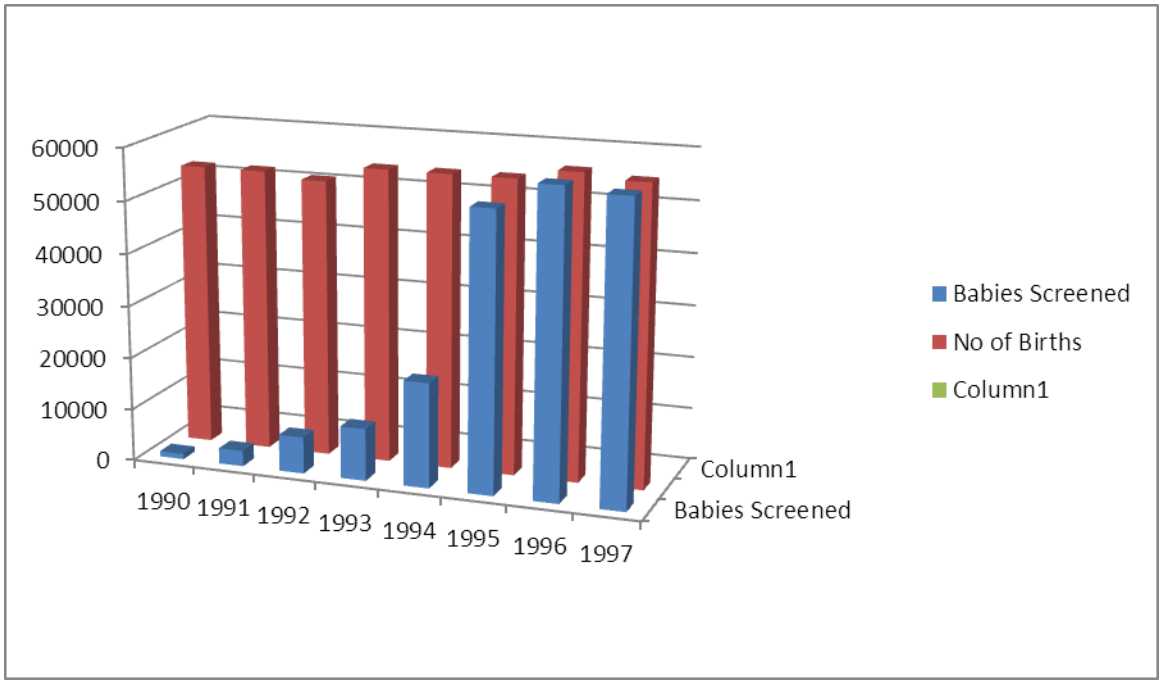
This alogrithm is unsuitable for NBS as sickling and solubility tests are not recommended for NBS because the minute amounts of haemoglobin S present in newborns are undetectable by such methods[Lane PA 2001, Kotila TR 2010].

3.2.3b Newborn Screening in SCD

The guideline advocates for NBS for SCD following evidence from developed countries on the potential benefits. It favours a voluntary rather than mandatory screening method and only after counselling has been provided and informed consent gotten from the child's parent. This is in contrast to the national policy on NCDs which requires mandatory screening. Considerations on ethical issues associated with mandatory screening may have influenced this modification.

The guideline advocates the need to extend coverage to babies born outside health facilities given that 62% of children are born at home[NDHS 2008]. Immunization centers are stated as strategic locations to achieve this goal given that the DPT1 immunization coverage is fairly good(about 59%). A similar strategy adopted in Uruguay(Figure 10) led to an increase coverage rate of NBS from about 36% in 1994 to almost 100% in 1997[Therrell 2003]. The guideline also recommends that strategic focal persons at all levels be made responsible for advocacy, mobilization and follow-up efforts for NBS.

Figure 10 :Comparison of newborns screened with births in Uruguay, 1990-1997.



Source: [Therrell 2003]

A moderately favourable policy environment exists for the introduction of NBS. The infrastructural organization of the health system seems to be lagging behind resulting in a policy implementation gap within the health system. The available resources may not be fully prepared for a nationwide scale of implementation and even if they were, NBS are usually commenced with pilot programmes.

3.2.4 Bill for the Prevention, Control and Management of SCD

This bill gives a comprehensive outline of SCD prevention, control and management. It advocates for a targeted approach of NBS for SCD in newborns whose mothers are carriers of the sickle gene or affected by the disease. However this approach will effectively miss many cases due to the low ANC coverage and facility births in the country. The bill also favours education of patients, patient families, providers and the public. It provides for treatment of affected persons, training of health professionals in genetic counselling and establishment of SCD registry and surveillance; measures which are enshrined in the recommended components of a standard NBS programme[table 2]. This bill however did not enjoy a majority vote among policy makers as they were unconvinced on why SCD should have a separate bill from the national health bill. Education of policy makers on the burden of disease and potential benefits of NBS in terms of improved clinical outcomes and cost savings for the country may modify this pattern of thought. A drawback in the bill is its proposition of directional counselling which advices at-risk couples not to marry each other and a denial of health privileges to affected kids of couples who ignore the advice. This constitutes an infringement on couples rights to association and reproduction, and injustice to the affected kids.

3.3 Context of Newborn Screening

This section will describe the context in which NBS exist with respect to political climate, regulatory framework, and societal values.

3.3.1 Political climate: Political climate connotes the sum total of the current mood and opinions about political issues that affect the population at any given time. The religious beliefs on inherited disorders across Nigeria as being an act of God may hamper the acceptance of screening programmes. The connotations in the northern part of the country which sometimes sees public health initiatives as plots by Western countries to achieve some 'hidden agenda' (as seen in the case of polio immunization[Yahya 2007]), can also affect introduction of screening programmes. The north-south disproportionalities in health indices as shown in ANC coverage[figure 2], immunization coverage[figure 3] and health workforce[table 4] which have been blamed on the relatively higher illiteracy and poverty levels in the north are issues which may influence the outcomes of NBS programmes.

3.3.2 Regulatory Framework: Newborn screening programmes operate within certain regulatory frameworks which guide their operations.

3.3.2a Ethical framework: The discussions on the ethical regulations of NBS have essentially focused around two opposing approaches to NBS: mandatory versus voluntary.[Ross 2010] Based on the tenet that the public health authorities have a responsibility to offer NBS to their citizens[Andermann et al 2010], the mandatory approach advocates that NBS be made compulsory by law for all conditions within the programme in a given state whether or not they meet the classical screening criteria.

The voluntary approach on the other hand insists that all NBS should be elective, requiring informed parental consent. A third approach is one that integrates mandatory screening for conditions amenable to treatment with elective or optional screening for conditions for which no known treatment exists but which are appropriate targets for biomedical research[President's Council on Bioethics 2008].
In the US[Therrell et al 2006] and some European Union countries[Cornel et al 2011] NBS is mandated by law in all states with an opt-out option available in most states except for five. For countries in other areas like the Middle East and North Africa(MENA] and sub-Saharan Africa where national screening programmes are is available, it is offered to all newborns with voluntary participation from parents.

3.3.2b Legal Framework: Legislation and regulation of NBS programmes are important in ensuring that screening is available to all who need it, meet required standards and that the best possible services within a given setting are provided. A Bill for SCD which seeks to provide the legal framework for its prevention, control and management is yet to gain approval by the national assembly in Nigeria. A policy to regulate early child hood hearing detection and intervention was developed for the country in 2004[WHO 2009] Although no national NBS law exist in the United States(US), all the 51 US NBS programmes have legal mandates that either established a NBS programme or allowed for its creation under a broader health mandate[Therrell et al 2006].

3.3.3 Societal Values: Social values are certain qualities and beliefs that are shared within a specific culture or group of people. These traits which include religion, culture and gender can influence the introduction of and way in which NBS is run in a giving context.

3.3.3a Religious: Religious views play a significant role in the understanding of, and attitudes towards the nature of genetic disorders[WHO 2006]. Appreciating the prevailing religious beliefs in any given setting is therefore critical to achieving effective and participatory genetic healthcare. The success of screening programmes partly depends on their acceptance by the religious and wider community. About two-fifths of individuals survey in a Nigerian study(both carriers and individuals affected by SCD) believed that the disease was an "act of God", even though most of them understood its mode of inheritance[Durosinmi et al 1995].
In the United States for example, even though NBS is mandatory in all states, 55 states allow parents to opt out of NBS for religious reasons while 5 do not[Therell et al 2006].
Many parents in Saudi Arabia cited religious explanations for causality of inherited genetic conditions; as they believed it was God who determined individual health status. However the belief did not prevent parents from seeking those treatments which the Islamic faith allowed[Panter-Brick 1991].

3.3.3b Cultural: Culture is a sum total of the beliefs, values and practices of a people. Genetic screening programmes need to be implemented in a manner which is sensitive to the cultural practices of any given population and maximizes the health benefits to patients and families[WHO 2006].
In Nigeria SCD has been culturally linked to reincarnation – "ogbanje" (among the Ibos), "abiku"(among the Yorubas). Due to the high mortality associated with the disease, and the inheritance pattern which runs in families, affected children are believed to "die and are born again" into their families in the current or in future generations[Nzewi 2001]. This can potentially hamper the desire for NBS among parents of affected children.
In respecting their cultural restriction toward prenatal diagnosis and/or abortion the Ashkenazi Jews developed a strictly confidential carrier screening programme for Tay Sachs disease amongst teenagers and then via a private match-making organization (Dor Yeshorim) couples who had no chance of passing on the disorder to their offspring were paired[Watson 1997]. The student screening programme for genetic blood disorders in Bahrain represents a different response to the potential discrimination of carriers in marriage. Here a cultural norm exists that girls who are found to be carriers may be unable to find husbands. The programme therefore relies on a system of comprehensive public education to address this culturally induced gender-based stigmatization and discrimination[Al Arrayed S et al 2003].

3.3.3c Gender: Gender is another relevant feature of the social context of genetic screening as traditional gender norms and gender inequality can affect reproductive decisions and patterns of discrimination within a community. Female who are either carriers of or affected by genetic diseases are often discriminated against in marriage[WHO 2006]. A female client of mine back in Nigeria told me her marriage to her fiancée was called off 3months before the wedding when he discovered she had SCD. In the study I co-authored, a third of high school students will not marry someone who has SCD[Olarewaju et al 2013]

CHAPTER 4: SCREENING CRITERIA AND STAKEHOLDERS INFLUENCE ON NEWBORN SCREENING

This chapter presents evidence to argue whether SCD meets the criteria to be included in NBS. It also examines the role that various key stakeholders play in influencing the introduction and/or expansion of NBS programmes in various contexts.

Deciding whether or not to introduce or expand population-based screening programmes is a complex venture and involves systematic analysis and synthesis of different kinds of evidence to evaluate the risks, benefits, and costs of screening from various view-points.[Andermann A et al, 2009] Availability of scientific evidence of effectiveness of screening programmes alone is no longer enough reason for its implementation, consequently the need for greater public engagement and debate about moral issues and societal values can not be over-emphasized. Using the study framework therefore, these complex issues are made more explicit and analysed in order to provide some guide toward a generally transparent and accountable consensus on policy decisions and implementation of NBS for SCD in Nigeria.

4.1 Screening Criteria and Principles

4.1.1 Improve health: To qualify for inclusion into a screening programme, there must be some health benefits attributable to early identification of and intervention on a disease i.e. the intervention should improve the health outcome of the individual(s) identified with the pre-symptomatic phase of such disease.

More than twenty years ago Vichinsky et al demonstrated the effectiveness of NBS for SCD[Vichinsky et al 1988]. The study showed that comprehensive care led to increased survival of children with SCD. Several other researchers have documented similar findings: a reduction in incidence of pneumococcal sepsis by 84%[Gatson et al 1986]; a reduction in SCD mortality from 15-30% to <1%[Griffiths et al 1988;Nussbaum et al 1984], a 99% chance of living at least 16years[Telfer et al, 2007].

Several pilot NBS programmes for SCD have commenced in a number of sub-Saharan African countries including Nigeria[JMDI 2009], Benin[Rahimy et al 2009], Burkinafaso[Kafando et al 2005], Ghana[Ohene-Frempong 2008], Democratic Republic of the Congo[Tshilolo et al 2009], but because the assessment for improved health outcome from such programmes is time-dependent, there is yet to be any documentation on the effectiveness of such interventions. Improved health outcomes were however observed when comprehensive care approach were used for symptomatic patients in a sub-Saharan African setting – Benin[Rahimy et al 2003]. A similar experience was observed in a Nigerian study where 'holistic care' for symptomatic patients (which involved the use of prophylactic antibiotics, pain medication, folic acid, routine immunization and parental education)

produced a significantly progressive reduction in morbidity and mortality rates[Akinyanju et al 2005].

4.1.2 Cost effective: Cost-effectiveness analysis(CEA) is a method for assessing the gains in health relative to the costs of different health interventions[Jamsion et al 2006]. It is used to determine which, among a range of alternatives, either: (i) maximizes the desirable outcomes given a fixed amount of resources, or (ii) minimized the cost in order to achieve a desired outcome[WHO 2006].
With respect to screening programs cost effectiveness is analysed in two ways: prospective and retrospective analysis[WHO 2006]. Prospective analysis examines the rationale for introducing a new screening programme based on data estimates from similar contexts. Cost effectiveness for fragile X carrier screening programme in Israel was based on such analysis with data from the Netherlands[Toledano-Alhadef et al 2001]. Retrospective analysis on the other hand justifies the continuation, modification or abortion of an existing screening programme by analysing data generated from the programme. Retrospective analysis done in 2004 for the prenatal screening for thalassaemia in Hong Kong showed a cost-effective programme[Leung et al 2004]. So did that done for the national NBS in Brazil four years after inception[WHO 2006].

Newborn screening for SCD is cost-effective when compared with symptomatic treatment. In a study done to calculate the cost to the UK National Health Service of providing treatment for patients with SCD, 0.57 to 1.25 early deaths per 100births were avoided as a result of early diagnosis through screening[Karnon et al 2000]. Rather than the cost effectiveness of NBS for SCD in general, the arguments have been that of comparative analysis of cost effectiveness of universal versus targeted/selective NBS. For laboratories to be cost-effective, they should be able to screen at least 25,000 births annually. At figures equal to or above 0.5 cases of SCD per 1000, no significant difference in detection component cost exist between universal and targeted NBS programmes[Davies et al, 2000]. Below this prevalence level a targeted programme is cheaper but is likely to miss cases. Universal screening on the other hand identifies more cases and prevents more deaths[Zeuner et al 1999; Panepinto et al 2000]. Based on studies in Benin and Burkina Faso, authors proposed the application of targeted screening for SCD in which selection based on mother's carrier status rather than ethnicity is adopted given the nearly even distribution of SCD prevalence (2%-3%) across different ethnicities in the sub-Saharan region[Rahimy et al 2003, Kafando et al 2005]. This targeted approach will miss a lot of cases in Nigeria as coverage for ANC (where the mothers will be screened) is about 64% on the average, and as low as 31% in the north-west zone of the country[figure 2].

4.1.3 Benefits versus harm: Screening programmes in general have the potential to do both good and harm. There is good evidence that early detection of SCD followed by prophylactic penicillin substantially reduces

the risk of serious infections during the first few years of life[Gatson et al 1986;Griffiths PD et al 1988;Nussbaum 1984]. Studies in Benin[Rahimy et al 2009], Ghana[Ohene-Frempong 2008], and Nigeria[Akinyanju et al 2005] have also shown improved health outcomes from application of comprehensive care to children affected by SCD. Additional benefits result from pneumococcal conjugate vaccination and parental education about early warning signs of infection and splenic sequestration. Finally the detection of SCD permits counselling for family members of affected child about disease management and future reproductive decisions[WHO 2006].
On the other hand NBS for SCD would identify healthy carriers who require primary health care workers to provide counseling[WHO 1996]. The incidental detection of sickle cell carrier status and haemoglobin disorders of questionable clinical significance has the potential to cause psychosocial harms, which may include exposure of non-paternity, stigma and discrimination against the child in education, insurance and employment, negative impact on self-esteem, and anxiety about future health[Working Party of the Clinical Genetics Society 1994]. Evidence shows that stigmatization and discrimination have resulted from confusion about the difference between carrying the sickle cell trait and SCD itself owing to lack of adequate public education and parental counseling[Farriaux&Dhondt 1994; Knoppers&Laberge 1990; Olarewaju et al 2013].

4.1.4 Respect human rights: Human rights require that NBS policies take appropriate account of, and observe widely respected human values concerning confidentiality, privacy and informed consent. The standard justification for mandating public health measures is that the measure will avert serious, imminent harm to others, but this does not apply to NBS[Baily & Murray 2008]. The rationale for screening without parental consent has been the minimal associated risk, the urgent need for early diagnosis, the great benefit of the treatment, the chance that the infant could lose this vital benefit if consent is denied[Baily&Murray 2008], and finally the tenet that public health authorities have a responsibility to offer NBS to their citizens[Andermann et al 2010]. Some authors argue that mandatory screening can be justified when the benefits of screening outweigh the risks/burdens[President's Council on Bioethics 2008]. A major reason for refusal of screening is poor parental knowledge[Campbell & Ross 2003]. The example of screening programme in Bahrain demonstrates how effective education campaigns can be in raising knowledge levels and avoiding some of these constraints[Al-Arrayed 2005; Al-Arrayed et al 2003]. A 99% acceptance rate for NBS for newborns whose mothers received post natal education and counselling was recorded in a Nigerian study[Odunvbun et al 2008]
To make provision for respect of human rights Ross[2010] proposes a tiered approach incorporating an opt-out process for conditions with a high benefit:risk ratio, an opt-in process for conditions with a more ambiguous benefit:risk ratio and additional tiers for permission for residual blood spot storage and research may provide the best way to

balance respect for parental autonomy and the promotion of children's health.

4.2 Key Stakeholders

Various key stakeholders have multiple influences on genetic screening policy decisions and implementation. Government driven political fiat are responsible in some instances. Support groups often influenced by citizens who had family members with the disease are responsible in others. And even in a few others the programmes are influenced by advisory committees of genetic experts on an evidence-informed platform. These multiple influences are now presented within different contextual settings.

4.2.1 Society: patient support groups, community groups and the general public

Social movements and interest groups have been known to exert great levels of influences on healthcare. Hiller et al [1997] have argued that the technical expertise of medical professionals puts them in no better pedestal than the lay public in making political and moral decisions concerning healthcare. The introduction and/or expansion of NBS programmes have been influenced by advocacy groups in the past including parent groups, patient advocacy groups, community groups and the general public[WHO 2006]. Parent's associations and community support groups have played a significant role in improving the treatment and population screening of beta-thalassaemia across the Mediterranean countries in the past two decades[WHO 2006]. The Cyprus Parent's Association has recorded a 97% success rate in decline of thalassaemia cases over a 10year period[Cao 1987]. Similar support groups which provide long-term support for affected persons, and work alongside regional and local genetic services include Jewish Care for Tay Sachs disease in the United Kingdom, Parents' Thalassaemia Association in Kurunegala-Sri Lanka[De Silva et al 2000], and the Thalassaemia International Federation for thalassaemia patients and parents from Cyprus, Italy, United Kingdom and United States[WHO 2006]. Paradoxical attitudes have also been observed as was the case when the French National Deaf Federation(Federation Nationale des Sourds de France) challenged infant hearing screening as an infringement on the cultural identity of the deaf[Dhondt 2010].

In Brazil the Cystic Fibrosis Brazilian Association has been influential in the development the National NBS Programme[Marques-de-Faria et al 2004]. The Sickle Cell Clubs in Nigeria are patient support and advocacy groups consisting of volunteers who promote SCD awareness, screening and work alongside with health facilities to promote the health of individuals affected by SCD as well as provide support for their families[Akinyanju 2009].

4.2.2 Medicine: Patients and families, Health professionals and Researchers

Various chronic diseases which contribute heavily to the global burden of disease have a genetic causal component. It is therefore rationale to expect that genetics and genomics will play a crucial role in their prevention and control in public health[Merikangas et al 2003].

The classical example of the influence of a health professional/researcher on screening can be traced to the efforts of Robert Guthrie in the development of NBS programmes. Motivated by his child's condition (mental retardion due to Phenylketonuria-PKU), he went ahead to develop an assay for phenylalanine in 1963 and this led to the introduction of NBS for PKU for which dietary interventions prevented the development of retardation in such children[Guthrie 1992]. Following this, the efforts of families whose kids had PKU (Association for Retarded Citizens) influenced the legislation of mandatory PKU screening across the US despite the absence of evidence to support the efficacy of such testing at the time[Therrell 2001].

The commencement of NBS for SCD in Ghana was initiated by Dr. Ohene-Frempong in 2003[Owusu 2010] while the pilot NBS for SCD in Nigeria was also influenced by Dr Inusa Baba, a Nigerian-born paediatric haematologist and researcher. A driving factor for such initiative was to promote research on SCD in Nigeria[JMDI 2009].

4.2.3 Industry: Biotechnology, Pharmaceutical and Biomedical

Industries in genetic medicine exert significant influence in screening programmes especially in areas of providing information, funding and innovations. Their commercial interests with regard to their efforts to introduce and/or expand genetic screening services may sometimes conflict with the best interest of patients. The tools via which these industries operate are highlighted here.

4.2.3a Direct-to-Customer Advertising. The print media, television and the internet are fast becoming alternate and sometimes even better sources of information for patients and their relatives. Industries provide both consumers and health professionals with valuable information about genetic testing availability and benefits. But sometimes they may overstate the value of genetic testing for consumer's clinical care. Furthermore such information may misinform consumers about genetic testing services, exaggerate their risks, and endorse a deterministic relationship between genes and disease. By appealing to themes of choice, hope, fear and peace of mind, these advertisements validate patients' worries about their genetic risks, heighten their expectations regarding the impact of genetics on their personal healthcare and appeal to their desire to assert demand for genetic screening services[Sarah et al 2002].

4.2.3b Using Patient Advocacy Groups: Increasing entanglement by with pharmaceutical and biotechnology companies have greatly influenced the public-health ethic of patient advocacy groups in adopting new rationales in their support of genetic screening services in favour of these

companies. Advocacy groups have become increasingly linked to industry. According to a Lancet editorial: "Many patients groups would not exist without funding from the pharmaceutical industry"[Editorial, 2006]. Infact some patient groups would not exist in the first place because they were actually created by these industries. In a Food and Drug Administration hearing, the head of an advocacy group urged approval of a medication for pancreatic cancer, stressing that she had no financial ties with the its manufacturer. Investigations into the matter however revealed the contrary[Kerr 2007].

4.24 Government: Health Sector and Other Sectors

It is the responsibility of national governments via their health governing bodies to assess and prioritize the health needs of their populations. Differences in the epidemiology, demographic factors and health systems in various countries reflect differences in public health policies and healthcare interventions including genetic screening services[WHO 2006].
As a response to limitations of the healthcare system in providing comprehensive care for newborns screened for PKU and congenital hypothyrodism, the Brazilian Ministry of Health established the National Newborn Screening Program (Programa Nacional de Triagem Neonatal, PNTN) in 2001. This was followed by a commitment by the Brazilian government in 2002 to provide resources for the early diagnosis, treatment and follow-up for disorders caused by inborn errors of metabolism[WHO 2006]. As a result of this commitment, over 13million newborns were screened between October 2001 and December 2005 representing a more than 50% rise in coverage from the data available in 2000. Similarly the Nigerian government via its health Ministry has committed to developing NBS programme within the country. Although they are yet to function at optimum capacity, six SCD centers have been established in the six geo-political zones of the country and will be used to run pilot-NBS programmes in each zone[FMOH 2012]. Also two states in the north-western part of Nigeria have adopted pilot NBS for SCD.

4.3 Values, Expectations, Preferences and Concerns.

4.3.1 Ethical: Ethics connotes the branch of philosophy concerned with the moral values and concepts of right or wrong and the justification for such judgements. In the medical parlance, bioethics refers to the study of ethical, social, philosophical and other related issues. The principles of autonomy, informed consent, privacy/confidentiality, beneficence, non-maleficence, and justice/equity are basic to any discussion of the ethics involved in genetic testing.

4.3.1a Autonomy connotes respecting the self-determination of individuals and protecting those persons with diminished autonomy. The respect of the autonomy (self-governance or independence) of individuals is paramount in virtually all ethical situations. One application of autonomy is informed consent, which includes discussion of purposes, potential benefits, risks and limitation of a specific genetic test and thereafter provision for voluntary participatory option. Newborn screening

programmes adopt the process of passive consent in which parents have the right to opt out of a particular mandatory screening test i.e. parents can refuse the test, however the absence of such refusal implies that they have consented to it. In this scenario the "informed" aspect of the informed consent concept is apparently silent. Mandatory NBS therefore raises serious issues of gaps in both education and knowledge necessary for adequate consent. Proponents for mandatory screening have argued that a voluntary participatory approach might lead to parents refusing this beneficial procedure for their children and ultimately lead to non-achievement of the goal of NBS[Baily, Murray 2008]. Available evidence has refuted this claim. Virtually all mothers who partook in a US based study supported NBS even in its mandatory form provided that NBS education is provided prenatally[Hasegawa et al 2011]. In Nigeria, a 99% acceptance rate for NBS was seen in mothers who participated in a hospital-based study. These mothers had received immediate post-natal NBS education and counselling[Odunvbun et al 2008]. Though the scope of educational information provided and the extent of benefits and risks of screening stated was not verified it suffices to suggest that adequate NBS education contributes to increased acceptance, favours voluntary participation and guarantees autonomy in such programmes.

4.3.1b Justice: Justice involves treating persons and groups equitably, and distributing benefits and burdens of health care as fairly as possible in society. The achievement of justice remains a core ethical issue in relation to the development of medical genetic services in developing countries. Justice is assessed on two main platforms: (i) balancing medical genetic services against other population health needs in terms of cost-effectiveness and (ii) equitable and safe access to medical genetic services once they have been introduced irrespective of socio-economic class, ethnicity, race or religion[WHO 2006].

i. balancing medical genetic services against other population health needs – It is crucial to consider this balance on a backdrop of the existing inequalities in the distribution of resources in global health interventions. Vast majority of the world's resources allocated for research are expended on tackling disease conditions that account for only a minute fraction of the global burden of disease. The "10/90 gap" refers to the fact that less than 10% of the global expenditure on health research and development is dedicated to the major healthcare problems that affect over 90% of the world's population[Lewis 2002]. Bringing this to the NBS perspective, huge and sometimes disproportionate health resources are often spent in research/interventions associated with the genetic screening of certain rare inborn errors of metabolism which affect only a minute fraction of the population. An example of this is seen in the United States state of Mississippi where huge amount of resources was invested into NBS for a rare inherited disorder known as medium chain acyl-coenzyme A dehydrogenase deficiency, or MCADD because of the advocacy efforts of a man who had lost his son to the disease[Baily & Murray 2008]. It is important to recognize that resources used in screening programmes have an opportunity cost

and that these resources could always be utilized in other forms of health interventions that improve the length and quality of human lives. Policy makers therefore have the ethical obligation to consider the implication of balancing medical genetic services against other population health needs (addressing the social, behavioural, and environmental determinants of health) when they make resource allocations decisions.

ii. Equitable and safe access to medical genetic services once they have been introduced. This is otherwise called distributive justice and connotes the fair, equitable and appropriate distribution of benefits and burdens within a society regardless of hierarchical divisions of social-economic strata, religion, race or ethnicity. Certain screening programmes are designed to target specific ethnic populations for no other morally justifiable reason except that the disease condition being screened for is common, but not restricted to that population. Screening for Tay-Sach's disease in some jurisdictions are designed to target populations of Ashkenazi Jewish origin[Kaback et al 1993], whereas haemoglobinopathy screening (specifically SCD) until lately were reserved for populations which trace their origin mainly from Africa.

4.3.1c Privacy and confidentiality: Privacy is said be violated in the event of unauthorized access to a patient's hospital record. By contrast a patient's right to confidentiality is said to infringed upon when an individual fails to protect or deliberately discloses personal information which the patient confides in him/her without the patient's consent[Beauchamp & Childress 1994]. The enactment of mandatory testing would decrease individual rights to privacy and possibly result in stigmatization and discrimination, a trend which is emerging in the mandatory pre-marital HIV screening required by some religious institutions in Nigeria[Uneke et al 2007]. Also the guarantee of privacy and confidentiality of patient's information by health professionals may be jeopardized in trying to strike a balance between safeguarding patient's interest and promoting public health benefits. Two moral theories – libertarianism and utilitarianism are considered in analysing such judgements. Liberitarians believe personal autonomy has the highest moral value, giving the individual the full rights to privacy, confidentiality and informed decision while expecting physicians to uphold patient's privacy rights at all times except in cases of mandatory reporting. The utilitarians on the other hand believe moral decisions should be made on the basis of burden/benefits estimations which promote societal good over individual benefit[Fulda&Lykens 2006].

In the United States, United Kingdom and many European countries full consent is a prerequisite to patient information disclosure. Peru and Argentina in South America, and Turkey in the Middle East uphold a more generic rather than genetic testing-focused patient's rights to confidentiality and privacy[WHO 2006]. No documentations were found on privacy and confidentiality issues in NBS for SCD in Nigeria however in my personal communication with Dr Baba Inusa (the initiator of the pilot NBS

for SCD) he said that privacy and confidentiality was maintained in the NBS programme as the results were only divulged to parents of affected infants and were kept confidential at all times. The HIV screening programme in the country however suffers occasional breach of privacy and confidentiality especially with respect to pre-marital screening[Uneke et al 2007]. Modell & Citrin[2002] suggest a balance between utilitarian and libertarian interests with regard to genetic testing arguing that the provider is morally justified to divulge confidential patient information if it has strong potential benefits to the patient's relatives, and the provider's advice to the patient to inform the relatives is not heeded.

Chapter 5: Discussion, Conclusion and Recommendations

5.1 Discussion

This chapter discusses the findings from the study based on the conceptual framework used. It also makes recommendations to relevant stakeholders based on available evidence.

Based on the clinical benefits that accrue from early identification and comprehensive care for affected infants, NBS for SCD has been shown to be clinically effective in high income countries. Some pilot studies also showed that it is technically feasible in low-middle income countries.

5.1.1 Health Policies and System

The policy on NCDs and the SCD guideline include interventions in SCD and NBS and therefore provide a platform for implementation of such interventions. However these policies are not being implemented. Policy implementation requires government commitment, funding and defined strategic actions. These requirements most often absent or weak and therefore result in policy-implementation gaps. Government's commitment to the Abuja declaration of "at least 15%" is therefore paramount.

This study shows that the Nigerian health system (including human and material resources and a functional HMIS) can greatly influence the introduction and/or expansion of NBS programmes and influence its outcome. Although the country workforce exceeds WHO recommended health workforce per population, they are inadequately skilled in genetic counselling and science, and HPLC laboratory diagnosis in SCD. This may be because genetics does not constitute a core component of the medical curriculum. Nevertheless a pool of counsellors exist in the HIV programme who can be trained in genetic counselling. So although pitfalls exist within the health system of the country, there is a window of opportunity for implementation of NBS programme.

5.1.2 Screening Criteria

As developed by Wilson and Jungner in 1968, criteria exist for inclusion of any disease into a NBS programme which border around availability of evidence of health improvement, cost-effectiveness, benefits-harm ratio and respect for human rights. This study has shown improved outcomes from NBS and comprehensive care for SCD in high income countries. Additionally good clinical outcomes were also seen among symptomatic patients who received comprehensive care in low-resource settings. The debates however are on cost effectiveness of NBS for SCD and this depends on a number of factors: the screening method applied (targeted or universal), the prevalence of the disease in a given population and the number of screening tests done per year. Within the Nigerian context the high disease prevalence(> 0.5 cases per 1000) supports a universal approach, however given the limited resources, a targeted approach in

which infants are selected based on their mother's carrier status may be more cost-effective. But since merely half of pregnant women attend ANC, a lot of cases will be missed by this targeted strategy. An alternative strategy is screening at immunization points. Integrating NBS with the already existing immunization program is cost-effective as it provides infrastructure, personnel as well as some level of coverage for NBS. Similar integration model increased NBS coverage in Uruguay by more than 150% over a 3-year period. A potential challenge to this strategy lies in the disproportionate levels of immunization coverage in the north compared to the southern part of the country, a situation blamed on information inadequacy and religious norms. Education is thus a key tool in this process. The Bahrain experience shows that active public education can influence norms and beliefs.

The study also shows that the benefits of NBS which is primarily aimed at the newborns outweigh the harm. Stigmatisation and discrimination are common and are sometimes targeted at the female gender especially in issues of marriage. The identification of non-paternity can also arise. Such findings at NBS may jeopardize the success of the programme. Education is again key in alleviating this issue.

In advocating for the respect of human rights, the more recent SCD guideline advocates for an informed consent based voluntary NBS as against the mandatory approach proposed in the earlier policy on NCDs. As shown in this study, with the experience in Nigeria[Odunvbun et al 2008], parents are unlikely to refuse NBS for their kids when adequate pre-test education and counselling is provided.

5.1.3 Key stakeholders

Key stakeholders have played very influential roles in the introduction of screening programmes across the globe as shown in the review. This study shows that patient support groups as well as patients and their families exert a potent force in favour of NBS. Sometimes their passion overrode considerations of clinical efficacy and diseases which did not meet the classical screening criteria made it into the NBS list [the MCADD case in Mississippi]. The ability of these advocacy groups to constitute themselves into strong political forces was used to their advantage and policy makers usually succumbed to their demands in order to maintain political relevance. Some advocacy groups actually campaign against NBS as shown in the French experience with NBS for hearing disorder.

The efforts of the sickle cell clubs in Nigeria led to the establishment of the SCFN, however they are yet to make similar impact on introduction of NBS for SCD. This may be due to lack of knowledge about NBS as it is still a relatively new field in Africa. Most pilot NBS initiated in Africa were by health professionals. These initiatives may have had a research motive or a desire to alleviate patients' sufferings.

Governments are also important actors especially in the area of infrastructural and staff support and regulating NBS programmes. The experience in Brazil and Ghana showed that government commitment is vital in facilitating the introduction of and ensuring a successful outcome in NBS.

5.1.4 Values, Expectations, Preferences, Concerns

This study shows that ethical, legal and social issues have gained prominence in NBS programmes and have come to be major determinants of its success beyond the application of the classical screening criteria.
Ethical issues such as autonomy and justice have featured prominently in NBS programmes.
Parental autonomy is clearly brought to light in the debate between mandatory versus voluntary NBS programmes. As identified in literature patient's right to autonomy seem to be violated by mandatory NBS programmes however some public health experts argue that public health authorities have a responsibility to offer NBS to their citizens[Andermann et al 2010] given the proven benefits of NBS. A balance is however created in availing parents an "opt-out" window which in most instances is passive and not clearly articulated. Justice in the equitable distribution of newborn screening service is desired in order provide such services to hard-to-reach areas. However this might have an effect on coverage and cost-effectiveness as services may be concentrated in in well-to-do settings and often times huge resources needed for other healthcare determinants may be used in tackling rare genetic disorders.
The social values of a given setting can greatly influence the introduction of a NBS programme. As shown in the review the religious and cultural beliefs in Nigeria which label SCD as an act of God and reincarnation respectively can mar the acceptability of NBS for SCD if the public's perception is not altered via education.

5.2 Conclusion

Given the proven benefits of NBS in improving health outcomes of affected children, a carefully planned and well implemented NBS for SCD in Nigeria has huge potential public health benefits. The introduction of NBS for SCD especially in Nigeria is affected by funding, education, health system preparedness (including human/material resources), government commitment, socio-cultural and religious beliefs and norms and influence of key stakeholders. Therefore analysis of these factors and how they influence the introduction and implementation of newborn screening is crucial to a successful outcome of the programme.

5.3 Recommendations

Following the discussions on the available evidence in this review, the following recommendations are made:

5.3a Education:

1. The FMOH should organize short courses on genetic counselling for existing primary healthcare workers (CHOs, nurses and midwives, doctors and other healthcare staff involved in providing counselling services e.g. HIV counsellors) as well as courses on genetic laboratory diagnosis for laboratory staff. Also health professional bodies should provide periodic opportunities for continuing medical

education to update members' knowledge on genetics and available genetic services.
2. Policy makers should incorporate medical genetics as a crucial component of medical training for all cadre of healthcare professionals as this will facilitate an acceptable level of understanding of genetics and genetic services.
3. FMOH, Federal Ministry of Education, healthcare workers and advocacy groups should develop and conduct educational campaigns to the general public as well as policy makers on NBS via community campaigns, mass media, schools and health centres to enlighten the general public about SCD and NBS.

5.3b Programme Design and Implementation:

1. The FMOH should definite and precise strategies that can ensure that the already existing policies on SCD and NBS are being implemented and ensure that HMIS for capturing data on SCD and other NCDs need to be strengthened to ensure proper monitoring and evaluation of the NBS programme
2. The NBS should be integrated into the existing child health programmes e.g. immunization especially in the southern part of the country. In the north where immunization coverage is low and more than four-fifths of births occur at home, traditional birth attendants (TBAs) can be trained to collect heel prick blood samples at delivery and send them to a centralized laboratory.
3. In order to deal with the challenge of tracking affected patients, community focal persons such as ward representatives and women leaders (who are well knowledgeable about the home addresses of members) should be involved in the tracking team.

5.3c Key stakeholders

1. Initiators of NBS should involve all key stakeholders (policy makers, religious and traditional leaders, patients and their families as well as advocacy groups) in the conception, planning and implementation of the programme.
2. The sickle cell clubs should be more informed on SCD and NBS and be better organized to influence policy makers' and government commitment to NBS programme and to fulfilling the Abuja declaration of 'at least 15%'.

5.3d Research

Research will be needed in the area of:

1. evaluating on-going pilot programmes in order to establish clinical effectiveness of NBS in low resource settings.
2. assessing the acceptability of the NBS programme by parents when it is introduced and the capacity of the health information system to be able to capture data on all aspects of the programme.

Appendix 1: References

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Appendix 2: Original Conceptual Framework of Andermann et al 2010.

Figure 1 Three tiers of a genetic screening programme

PROGRAM MANAGEMENT LEVEL
Governance (define regulations, manage resources, organize services, measure outcomes, assure quality control)
Resources (human, technological, structural, financial, information)
Services (recruitment, informed consent, offer of screening, provision of counselling, offer of interventions, provision of follow-up)
Outcomes (morbidity & mortality, quality of life, reproductive choice, clinical validity and utility, satisfaction, psychosocial impact)
Quality control (management level, clinical level, laboratory level)
CLINICAL SERVICES LEVEL
Screening type (mass, opportunistic, cascade)
Population (universal, selective)
Disease (monogenic, multifactorial, chromosomal, mitochondrial)
Test (presymptomatic, predisposition, susceptibility, carrier, pharmacogenetic)
Intervention (prevention, early treatment, family planning)
LABORATORY TESTING LEVEL
Personal disease risk** (presymptomatic = high, predisposition = moderate, susceptibility = low, carrier = not at personal risk)
Timing (preconception, preimplantation, prenatal, neonatal, child, adult)
Method (molecular, cytogenetic, biochemical, imaging)
Validity (analytical validity, clinical validity)

Figure 2: Multiple influences on genetic screening policy decisions throughout the life cycle of the programme

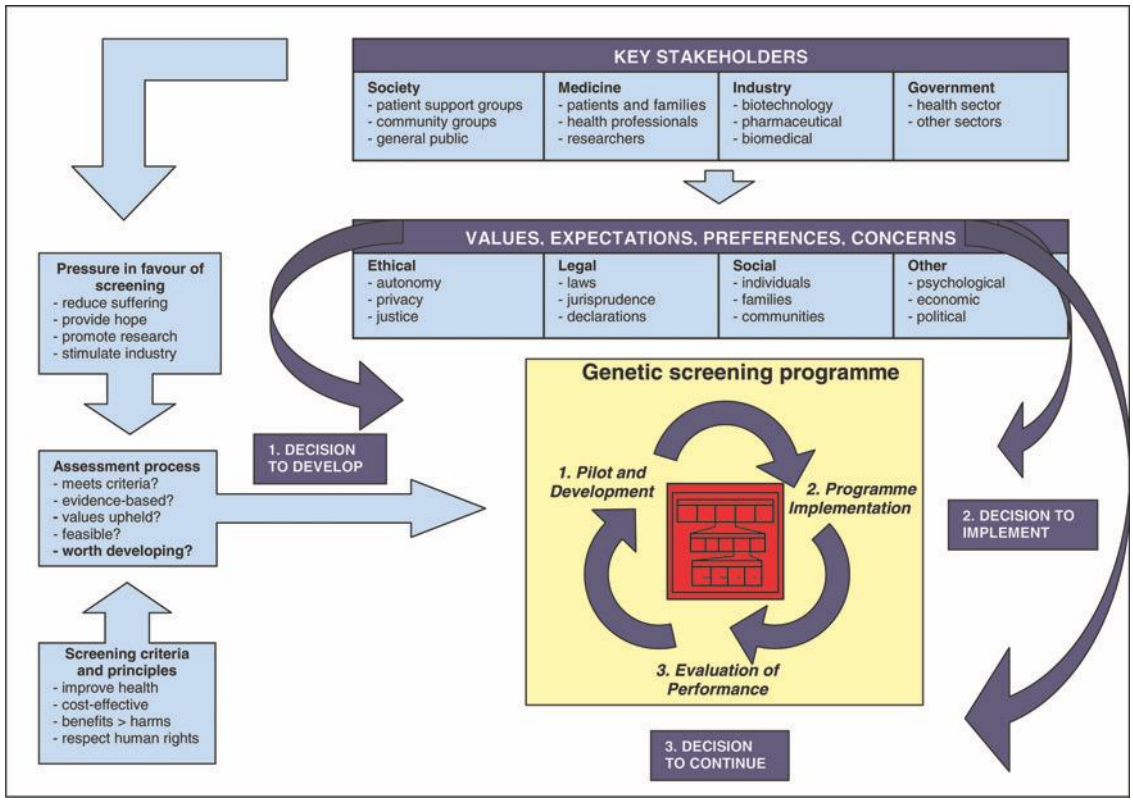
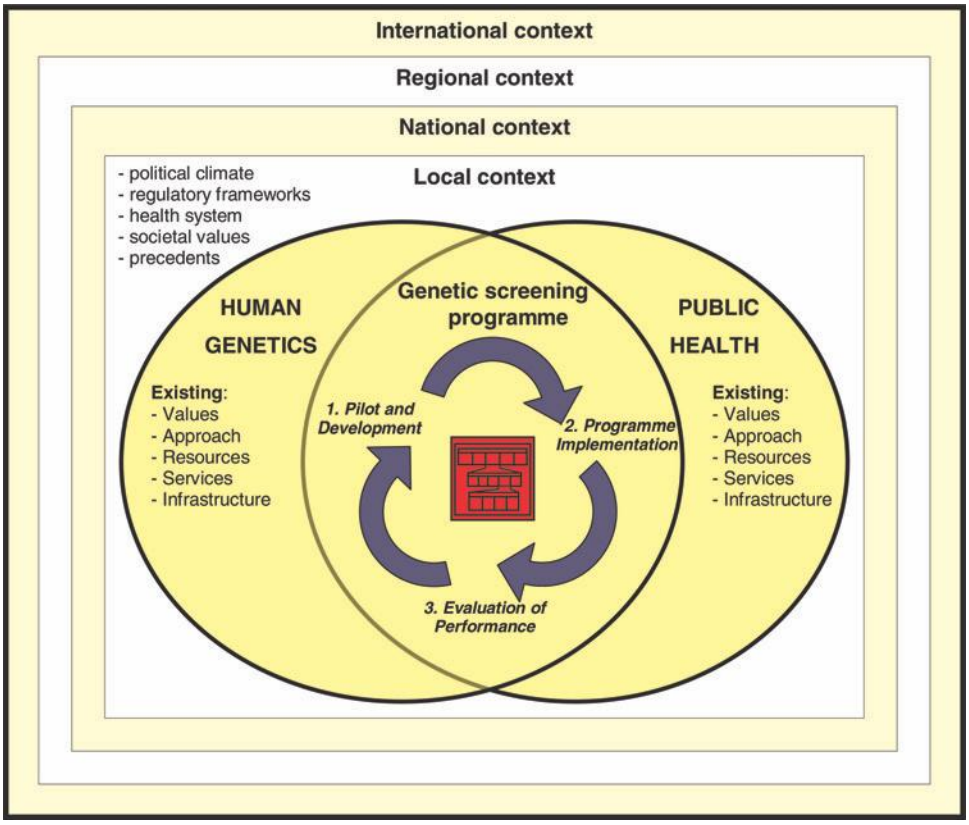


Figure 3: Multi-layered context for genetic screening policy-making



Appendix 3: Wilson and Jungner Screening Criteria

Box 1. Wilson and Jungner classic screening criteria1

1. The condition sought should be an important health problem.

2. There should be an accepted treatment for patients with recognized disease.

3. Facilities for diagnosis and treatment should be available.

4. There should be a recognizable latent or early symptomatic stage.

5. There should be a suitable test or examination.

6. The test should be acceptable to the population.

7. The natural history of the condition, including development from latent to declared disease,

should be adequately understood.

8. There should be an agreed policy on whom to treat as patients.

9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be

economically balanced in relation to possible expenditure on medical care as a whole.

Appendix 4: Bill for the Prevention, Control and Management of Sickle Cell Disease

A BILL

FOR

An ACT To Provide For The Prevention, Control And Management Of Sickle Cell Disease And For Other Purposes Connected Therewith

Sponsored by SEN. (DR) IFEANYI OKOWA
SEN. USMAN NENADI E.

Co – sponsors:

SEN. SARAKI, ABUBAKAR O.
SEN. NGIGE, CHRIS N.
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SEN. KAKA ADEGBENGA SEFIU
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SEN. MARAFA, KABIR GARBA
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SEN. EZE, AYOGU
SEN. TANIMU, PHILIP ADUDA
SEN. TINUBU OLUREMI SHADE
SEN. ADEYEMI SMART
SEN. OBADARA OLUGBENGA ONAOLAPO
SEN. LAR VICTOR
SEN. ADENIYI ANTHONY A.
SEN. ENANG ITA SOLOMON J
SEN. NWANGWU MATTHEW IFEANYI

]

BE IT ENACTED BY THE NATIONAL ASSEMBLY OF THE FEDERAL REPUBLIC OF NIGERIA-

PART 1- ESTABLISHMENT OF A SICKLE CELL DISEASE PREVENTION, CONTROL AND MANAGEMENT PROGRAMME.

1. The Government of the Federation shall engage in and encourage the prevention and control of the occurrence and spread of Sickle Cell Disease, hereinafter called
   ‘’the Disease’’, in the manner provided for in this Act
   (2) The Government of the Federation shall provide support for patients suffering from the disease by way of a treatment programme and other forms of support as may be determined with time, while encouraging enhanced research to identify next-generation treatment.
   (3)The Government of the Federation shall encourage the participation of all States and Local Governments in the programme.

2. (1) Any person or group in the federation may, subject to any restriction or requirement under this Act, freely participate in the prevention, control and management of the occurrence, spread and effect of the disease.

(2) Subject to any law relating to information dissemination or any restrictions arising from this Act, any person or group may give, disseminate or distribute appropriate information or literature useful in the prevention, control and management of the disease.

3. (1) The prevention, control and management of the disease (hereinafter referred to as ''the Programme'') as provided for under this Act, shall be directed, coordinated and supervised by the Ministry of the Government in charge of health, hereinafter referred to as ''the Ministry''.

(2) The functions and duties of the Ministry in respect of this programme shall include-

(a) The establishment and coordination of a Sickle Cell Screening programme, with counselling by trained individuals with specific knowledge of the disease.

(b) Provide and improve access to quality care for Sickle Cell Disease patients. Linking laboratory results in deliverable ways to the provision of clinical care by creating properly staffed approved local health institutions.

(c) Raising awareness about the disease at local, national and governmental levels.

(d) Ensuring programme support from governmental and non-governmental organizations, including private companies.

(e) Advocacy to draw the attention of international health agencies to the public health problem and cost burden, with a view to attracting international collaborative assistance.

(f) Developing a data base of Trait carrier frequency and disease prevalence for evidence based planning and calculation of burden of disease. Clinical data on patterns of disease presentation, treatment regime and treatment outcome shall be collated and audited.

(g) Managing clinical networks adapted to local needs and resource availability and the building of care networks into existing hospital services. Enhancement of partnership between primary care clinics and community based Sickle Cell Disease organizations.

(h) Improve and expand patient, patient family and provider education.

(i) Ensure continuity and coordination of service delivery for individuals with the disease.

(j) Such other functions and duties that are provided for it under this Act.

(3) Any of the foregoing functions or duties of the Ministry in respect of the programme may be performed or discharged by the Ministry directly or through any appropriate agency thereof.

PART 11- ACCREDITATION OF CENTRES AND PARTICIPANTS

4. (1) In furtherance of Section 3(2) (b) of this Act, the Ministry may accredit public and private hospitals and medical clinics or health centres (hereinafter referred to as '' the Centre'') for the purpose of implementation of the programme. Such centres shall-

(a) Serve for the provision of medical treatment for the disease

(b) Provide for genetic counselling and blood genotype testing of the public

(c) Keep, collate and transmit to the Ministry or its designated agency monthly or periodic records of persons who have undergone genotype test, genetic counselling and medical treatment for the disease. Such records shall include the names, age, addresses of the persons attended to and the dates of visit.

(d) Keep a register of all Sickle Cell patients, as well as that of carriers.

(2) In accrediting the centres under this section, the Ministry shall ensure that-

(a) There is a fair distribution of accredited centres in each State of the federation; and

(b) The centres are so selected in each State as to ensure the easy access of people from every part of the State to the services rendered by the programme.

(3) The Ministry or its designated agency may pay to the accredited centres for the performance of any of their duties herein provided, such fee or remuneration as shall be determined by the Ministry or the designated agency

(4) A private hospital or medical clinic shall not be accredited by the Ministry under this section or any provision of this Act if-

(a) The hospital or clinic is not registered with the appropriate government authority

(b) The owner, proprietor or head of such hospital or clinic has been found guilty of professional misconduct or convicted of a criminal offence of which he has not been discharged off.

(c) In the opinion of the Ministry the centre is of low standard and may not be able to provide the required services.

(5) No action or claim shall lie against the Ministry for any refusal to accredit any health institution under this Act.

5. (1) There is hereby established under this Act a National Coordinating Centre for the Sickle Cell Disease control programme

(2) The National Coordinating Centre shall reside in the National Primary Health Care Development Agency (NPHCDA). It shall be a substantive department in the Agency, without prejudice to the Act initially establishing the Agency.

(3) The National Coordinating Centre shall-

(a) Collect, coordinate, monitor and distribute data, best practices, and findings regarding the programme;

(b) Develop a model protocol for eligible centres with respect to the prevention and treatment of the disease;

(c) Develop educational materials regarding the prevention and treatment of the disease

(d) Prepare and submit through the Ministry to the National Assembly annually a report that includes recommendations regarding the effectiveness of the programme under this Act and such report shall include direct outcome measures as—

(i) The number and type of health care resources utilized (such as emergency room visits, hospital visits, length of stay, physician visits for individuals with the disease); and

(ii) The number of persons that were tested and subsequently received genetic counselling for the sickle cell trait.

(4) The head of the coordinating centre shall be the Director of the Programme. The director shall be assisted by other staff as the Governing Council may approve for the programme.

6. (1) The Ministry through its agency in further pursuance of section 3(2) (d, g) of this Act shall encourage and accredit local or foreign or private non-governmental organization or bodies to partner with it on the sickle cell programme;

(2) The organization or bodies so accredited in the programme may without cost or charge to any member of the public –

(a) Procure, obtain and disseminate or distribute appropriate information or literature relating to the prevention, control and management of the disease.

(b) Procure, receive and distribute approved drugs for the management of the disease to accredited health institutions, the Agency or Ministry;

(c) Carry out enlightenment campaigns to support the programme, as well as advocate for and encourage genetic testing by members of the public including but not restricted to intending couples.

(d) With the approval or upon the request of the Ministry or its agency carry out any special function or activity in support of the programme.

PART III - ESTABLISHMENT OF REGISTRY

7. The establishment of a Sickle Cell Disease Registry and a Surveillance System is authorized under this Act.

(1) The goal of this initiative is to establish a sickle cell data system that will be used to describe the epidemiology and characteristics of the disease;

(2) This data can be used for research, information dissemination, policy decisions, and health care planning at the local, state and national levels.

PART IV – STRATEGIC COMPONENTS OF THE PROGRAMME

8. The main components of the Sickle Cell Disease prevention, control and management programme shall include –

(1) The Sickle Cell Disease Newborn Screening Programme (SCD-NBS). The screening of all newborn of mothers who are identified carriers of the sickle cell trait or suffering from the disease shall be encouraged and provided for under this Act.
(2) The genetic testing of parents or other appropriate relatives of children with Sickle Cell Disease and of adults with the disease.
(3) The genetic testing of all pregnant mothers is to be encouraged under this Act, as this will give effect to section 8 (1) of this section.
(4) Genetic counselling and testing, particularly of intending couples
(5) Primary and secondary preventive medical strategies including prophylaxis, and treatment and services for individuals who have sickle cell disease.
(6) Training of health professionals (including doctors, nurses and other health staff) on genetic counselling.
(7) Education of parents and family members of persons suffering from the disease in counselling programmes
(8) The free treatment of the complications of the sickle cell disease in this programme shall come into effect when the National Health Fund is established. It shall then be financed from the fund without prejudice to the Act establishing the FUND.
(9) The Government of the Federation in collaboration with the States shall encourage the education of children born with the disease at least to the senior secondary school level.

PART V – ESTABLISHMENT OF GOVERNING BODY

9. (1) There shall be for the Programme a governing body to be known as'' the Council '' which shall have the responsibility for the general supervision and provision of guidelines for the control of Expenditure of the programme.

(2) The Council established pursuant to subsection (1) of this section shall consist of the following members –

(a) The Minister of Health, who shall be the Chairman
(b) The Minister of State for Health, who shall be Vice-Chairman
(c) The Executive Director, National Primary Health Care Development Agency
(d) The Head of National Coordinating Centre, who shall be the Secretary
(e) The Director, Planning, Research and Statistics of the Ministry
(f) A haematologist and a Sickle Cell Disease expert from tertiary health institution
(g) A representative each of the Ministers for Education and that in charge of Women Affairs.
(h) Two other Nigerians (one of whom must be a woman) who have or are members of a non – governmental organisation working in the control and management of sickle cell disease.

(3) (a) The members of the council who are not ex- officio members shall be appointed by the minister in charge of health.

(b) The members of council shall be paid sitting allowances as may be approved, but not beyond that earned by part – time members of boards in federal parastatals.

(4) (a) A member of council appointed otherwise than by office, shall hold office for period of four years, and may be eligible for re – appointment for one further term of four years.

(b) The office of a member of council shall become vacant if: -

(i) He resigns as a member of the Council in writing under his hand addressed to the minister; or

(ii) The Minister is satisfied that it is not in the interest of the Council for the person appointed to continue in office, and notifies the person to that effect.

(5) Apart from providing general supervision and guidelines for programme expenditure, the Council shall ensure –

(a) The allocation of resources to support the publication and dissemination of educational materials;

(b) provision of funding for counsellor certification programmes;

(c) The allocation of resources for all strategic components of the programme;

(d) The encouragement of the creation of sickle cell disease clinical research networks.

(e) That measures that may prevent the dropping out of school of individuals suffering from the disease are planned for as the programme funding improves.

(6) The Council shall have supervisory authority over the programme and shall exercise the following powers:

(a) Appointment and discipline of Director of the programme.

(b) Approval and ratification of appointments, promotion and discipline of other staff of the programme.

(c) Approval of the draft budget of the programme before it shall be sent for appropriation

(d) Make regulations and guidelines for the operation of the sickle cell programme.

(e) Approve the accreditation and de-accreditation of centres in States.

(f) Approve relevant units to be headed by Deputy/Assistant directors, who shall work under the leadership of the Director of programme.

(g) Establish a Management Committee which shall include the Executive Director of NPHCDA, Directors and Deputy/Assistant Directors of the Programme, under the leadership of the Executive Director.

(h) Take any action necessary for the effective implementation of the programme.

(7) (a) Council shall meet quarterly to review progress of the implementation of the programme; and consider and approve request from the management committee and any other issue it may find necessary.

(b) Extra ordinary meetings may however be convened by the Chairman, and if the Chairman is requested to do so by notice given to him by not less than six members of the council

(c) The chairman shall preside over every meeting and in his absence, the Vice Chairman shall preside.

(d) The Council shall meet to conduct its business at such place and such day as the Chairman may appoint, and the quorum for all meetings shall be six members.

(e) The Council shall have the power to invite or co-opt any person to attend its meetings. Such person shall participate in the proceedings of the meeting, but shall not be entitled to vote.

(f) The Council may appoint one or more Committees to carry out on its behalf such functions as the Council may determine.

(g) A Committee appointed under sub-section (7f) shall be presided over by a member of Council and consist of such persons (not necessarily all members of the council) as may be determined by the Council.

(h) A decision of the Committee of the council shall not have effect unless confirmed by the Council.

PART VI – FINANCIAL PROVISIONS

10. (1) The programme shall establish a fund from which shall be defrayed all expenditure incurred in the running of the programme for the purpose of this Act.

(2) There shall be paid and credited to the fund of the programme-

(a) Budgetary allocations from the Federal Government.

(b) Grants from State and Local Governments.

(c) Foreign aids and assistance from bilateral agencies and bodies.

(d) Donations from persons, local organizations and Cooperate bodies.

11. The Ministry through the National Coordinating Centre shall from time to time, apply the funds at its disposal to:

(a) The maintenance of its office.

(b) Pay allowances and other benefits of members of council and its committees.

(c) Pay the emoluments and entitlements of the director and other members of staff of the programme.

(d) Pay overhead, allowances, benefits and other administrative costs of the programme.

(e) Ensure the implementation of the components as outlined in section 8 (1-7) of the Act.

(f) Undertake any other activity in connection with or likely to enhance the success of the programme.

12. All income derived by the programme from the sources specified in section 10 (2) of this Act shall be exempted from income tax and all contributions to the fund of the programme shall be tax deductible.

13. The National Coordinating Centre shall through the Council submit its income and expenditure for the following year to the minister not later than 30th September each year.

14. (1) The Ministry may, subject to section 15 of this Act, receive donations of funds, drugs, literature or other materials from persons, organizations, bodies or governments for the programme.

(2) The Ministry shall keep a record of all such donations made to it under this Act.

(3) The Ministry shall give annual reports of such donations and its utilization in the programme activities to the National Assembly in such details as may be required

(4) The Ministry of Health or through the Governing Council, National Coordinating Centre or accredited Centres may receive drugs in donation for the treatment of complications of the disease. Such medications shall be administered free to sick patients with the disease.

15. (1) The Ministry shall, before accepting any donations of drugs, literature or other materials ensure-

(a) In the case of drugs that they are relevant to the programme and of proven efficacy;

(b) In the case of literature and other materials, that they are relevant and appropriate for the prevention and/or management of the disease.

(2) The Ministry shall not accept any funds donated or intended to be donated to it if it knows or has reason to believe that the funds are illegally or unlawfully acquired.

(3) The Ministry shall not receive any drugs, literature or other materials donated if it knows or is of the opinion or has reason to believe that such drugs, literature or material is illegally or unlawfully acquired.

(4) Where the Ministry refuses or declines to accept any donations for any of the foregoing provisions, it shall in writing inform the donor or donors concerned, availing it of the reasons for the refusal.

PART VII–STAFF OF THE NATIONAL COORDINATING CENTRE

16. There shall be appointed for the National Coordinating Centre a Director of Programme, who shall be appointed by the governing council.

(1) The Director of Programme shall subject to general control of the Council and be:

(a) Responsible for the implementation of the day to day administration of the affairs of the programme.

(b) Responsible for the keeping of proper records of the proceedings of the Council; and

(c) The head of the programme and be responsible for the administration thereof and the direction and control of all other employees of the programme with the approval of the Council.

(2) The Director of the programme shall hold office for four years and may be eligible for re-appointment for a further term of four years.

17. The Council shall have power to appoint directly or by transfer or on secondment from the public service in the federation, such number of employees, as may in the opinion of the Council, be required to assist in the discharge of functions of the National Coordinating Centre under this Act.

(1) The terms and conditions of service (including remuneration, allowance, pension, gratuities and other benefits) of the persons employed by the Council for the centre shall be as determined by the council, but as applicable in the civil service of the federation.

18. (1)The Council may, subject to the provisions of this Act, make staff regulations relating generally to the conditions of service of the employees of the centre and without prejudice to the generality of the foregoing, such regulations may provide for -

(a) The appointment, promotion and discipline (including dismissal) of employees of the centre.

(2) All such regulations must be as applicable to those in the civil service of the federation.

19. It is hereby declared that service in the National Coordinating Centre shall be public Service for the purposes of the Pensions Reform Act 2004 and, accordingly, officers and other persons employed in the centre shall, in respect of their service in the centre, be entitled to pension, gratuities and other retirement benefits as are prescribed there under, so however that nothing in the Act shall prevent the appointment of a person to any office on terms which preclude the grant of a pension or gratuity in respect of that office.

PART VIII – SPECIAL SERVICES TO INTENDING COUPLES

20. (1) Accredited centres under this Act shall run special services for persons intending to get married to each other. Such services shall include–

(a) Carrying out of genotype tests;

(b) Genetic counselling particularly for those that are carriers of the sickle cell trait or have the sickle cell disease.

(2) Where it is learnt or found through genotype test that intending couples may bear children prone to the disease, the medical personnel or centre attending to the couple shall –

(a) Advise such intending couple not to go into the marriage due to the likelihood of occurrence of the disease in children that may be born there under;

(b) Reduce such advice in writing and issue the written advice to the persons concerned and keep records of the full names, addresses and other particulars of such persons so counselled.

(3) No action or claim for breach of promise to marry shall be brought against anyone withdrawing from an intended or planned marriage in compliance with a written advice of an appropriate medical personnel under subsection (2) of this section.

(4) Notwithstanding anything to the contrary in any provision of this Act –

(a) No intending couple shall be forced to comply with the written advice of a medical personnel

(b) The couple in marriage shall however bear the burden of medical services of all children born with the disease in such marriage.

(5) Nothing in this section or any provision of this Act shall be construed to warrant, support or justify any divorce or withdrawal by any person from an already subsisting lawful marriage or from any obligation there under.

PART IX – MISCELLANEOUS PROVISIONS

21. (1) The Ministry may specially assign or request any non-governmental organization or body accredited by it to carry out awareness, enlightenment and education campaign or advocacy or to perform any specified function permitted by this Act for the prevention and control of the disease in the federation or any part thereof.

(2) Where the Ministry specially assigns an accredited organization or body any specified activity in accordance with this section, it may make available to the organization or body the resources and materials which the Ministry considers necessary for the performance of that activity.

22. The accreditation by the Ministry of any centre, organization or body under this Act may be withdrawn or cancelled where such centre, organization or body –

(a) Does not satisfactorily perform its functions or those assigned to it by the Ministry under this Act ;

(b) Has become affected by any of the disqualifications from accreditation under this Act or was not qualified for accreditation under this Act at the time it was accredited ;

(c) Diverts to its private use or is found to be unfair in the dispensation or administration of any drugs or material or any part thereof made available or donated to it for the benefit of the public.

(d) Is in breach of or acts contrary to any clear provisions of this Act or any of the terms of its accreditation under this Act ;

(e) Is in breach of any of its functions or duties or the terms of any specific or special functions assigned to it by the Ministry under this Act.

23. The Ministry may directly or through any of its agencies make available or distribute all drugs, literature or materials in its possession for the programme or make some or any quantity thereof available to the accredited centres, organization or body to administer or distribute to members of the public.

24. Where an offence is committed under this Act in respect of any funds, drugs, literature or material, such funds, drugs, literature or material shall be forfeited to the government of the federation which shall remit same to the Ministry and the funds, drugs, literature or material shall be deemed as donated to the Ministry.

25. (1) Anyone who diverts or appropriates funds for his or her private use or sells or diverts drugs, literature or material meant for the programme under this Act commits an offence ;

(2) Any person who diverts or converts to his or her private use funds, drugs, literature or material meant or despatched for donation to the Ministry or any of its agencies or centres, organization or body in respect of the programme commits an offence.

(3) Any person who commits an offence under this section shall be liable on conviction to a term of imprisonment of two years or a fine of one hundred thousand Naira (N100, 000).

26. In this Act:-

"The disease" means Sickle Cell Disease

"The programme" means the prevention, control and management of Sickle Cell Disease

"The Ministry'' means the Ministry of the Federal Government in charge of health.

''The centre'' means any hospital, clinic or health institution accredited for the programme

"Minister" means Minister in charge of health.

27. This Act may be cited as "Sickle Cell Disease (Prevention, Control and Management) Bill, 2011".

EXPLANATORY MEMORANDUM:

This Bill seeks to provide a legal framework for the prevention, control and management of sickle cell disease and to draw the attention of the public to the health burden arising from the disease in Nigeria.