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An Evidence-Based Policy Brief

Development of a national package for management of Sickle Cell Disorders

Executive Summary

Included:

- *Description of sickle cell disorders problem*
- *Viable options for addressing this problem*
- *Strategies for implementing these options*

Not included: recommendations

This policy brief does not make recommendations regarding which policy option to choose

Who is this policy brief for?

Policymakers, their support staff, and other stakeholders with an interest in the problem addressed by this policy brief

Why was this policy brief prepared?

To **inform deliberations** about health policies and programmes by **summarizing the best available evidence** about the problem and viable solutions

What is an evidence-based policy brief?

Evidence-based policy briefs bring together **global research evidence** (from systematic reviews*) and **local evidence** to inform deliberations about health policies and programmes

***Systematic Review:** A summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise the relevant research, and to collect and analyse data from this research

Full Report

The evidence summarised in this Executive Summary is described in more detail in the Full Report

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Key messages

The problem:

Sudan lacks a national comprehensive package for prevention and management of Sickle Cell disorders (SCD) that led to the following:

- Deficiency of epidemiological data that reflect the magnitude of the problem.
- Absence of a national protocol for SCD management which resulted in poor clinical course and outcomes.
- Unavailability of Some diagnostics techniques important for proper disease management
- Unavailability of SCD drugs due to interruptive supply and high cost.
- Most health cadres are not well trained to deal with SCD.
- Social misbelieves and absence of health education are among the factors that escalate patients grievances
- As consequence to the above mentioned factors, SCD patients have very poor school attendance and performance.

Policy options:

The national package for prevention and management of SCD has to entail the following elements; screening, nationwide management protocol, access to the appropriate medication and diagnostics services, patient counseling and community awareness and partnership. This package can be introduced through the following options:

Option 1: development of a national program for management and reduction of morbidity and mortality of SCD:

This option focuses on integration of SCD management in all health system levels, introduction of screening, health insurance for SCD patients and community participation and empowerment. Major strengths:

- Holistic and comprehensive approach to problem solution
- Promote equity, quality and access

Option2: establishment of integrated centres of excellence for management of SCD.

This option focuses on establishment of integrated SCD centres in three states while linking it to a national reference centre at the capital. Major strength:

- More feasible and easy to implement
- Promote quality and access in states of high prevalence

Implementation barriers:

Barriers to the above mentioned options are categorized as follows

- Disease is prevalent in hard to reach population.
- Health providers' unavailability and their limited capacity in SCD management and team working
- Weak existing health information, research and referral systems
- The growing disinterest of health system leaders in development of new national control programs.
- SCD is not a priority among national or international initiatives.

Implementation strategies:

- Improvement of patients' access by health insurance enrolment and comprehensive community awareness programs
- Training, multidisciplinary team building, and advocacy among existing staff and mobilize states to fill human resources for health gaps
- Develop simple information and referral materials while integrating with existing successful systems.
- Develop priority SCD research and advocate for it.
- Advocacy about the problem nationally and internationally.

Executive summary

The problem

SCD is a devastating non-communicable disease that lacks global as well as national attention; it has huge impact on affected communities' health, psychology and economic status. It causes deformation of the red blood cells that can result in vaso-occlusive events which causes a range of manifestations; pain crisis, ischemia and tissue and organ damage. These complications might be fatal such as the acute chest syndrome [1]. Frequency of some of these manifestations is associated with low life expectancy**.**

Lack of systematic national attention to SCD prevention and management caused inexistence of recent information about the disease burden and epidemiology. Other than the studies conducted more than thirty years ago and observations of the practicing pediatricians mainly, in Abnaof SCD clinic in Khartoum, there is no exact information about the disease. Patient's access to proper management is a challenge due to the insecurity problem in some of the affected areas and patients characteristics as most of them are nomadic, illiterate, and of low socioeconomic status. There is no national protocol for disease management and major disease prevention and management innovations are not in practice. Disease diagnostics like electrophoresis machines and simple management measures like blood transfusion are lacking especially in rural areas where the disease is highly prevalent.

In conclusion SCD affected community are lacking services availability and accessibility. Children with disease are subject of continuous disease complications that limit the quality of their life, burden their families and society and threaten their life.

Policy Options

With regards to introduction of a national package for SCD prevention and management, there are two options to be considered. The first is about development of a national program

for SCD prevention and management. This option implies more investment on PHC, secondary and tertiary facilities, human resources training as well as logistics and management support. The second option calls for development of centres of excellence mainly in the affected states. These centres should be coordinated and governed by a national centre at Khartoum state.

Option 1: development of a national program for management and reduction of morbidity and mortality of SCD:

This option focuses on development of a national protocol for management of SCD, introduction of SCD screening and community awareness, integration of management services in primary, secondary and tertiary levels of the health system, enrolment of SCD patients and families in social health insurance system combined with supporting management structure at state and national levels. Major strengths of this option is that it promotes quality of services and patients access to services either geographically or financially. Furthermore, it addresses the SCD problem in a comprehensive manner; both at health services and community levels. However, this option is a bit costly compared to the second option and need coordination with other sectors.

Option2: establishment of integrated centres of excellence for management of SCD.

This option like option one incorporates development of a national protocol for management of SCD and screening, patient counseling and community awareness. However, it focuses on establishment of an integrated SCD centres in three states while linking it to a national reference centre at the capital. Major strength of this option is that it improves quality of care provided to SCD patients, it can act as piloting for development of national program. However, this option is limited in addressing patients access to care especially in other states. It also, might interfere with the recent national health services policy

Implementation barriers and strategies

Adoption of each of the two above mentioned options require implementation of different interventions to deal with different barriers for success. These barriers pertain to health system weaknesses, stakeholders' reaction to options, health providers and patients and community limitations. Major barriers to both options can be summarized as follow:

1. Patients' characteristics are a major barrier for both options implementation. SCD is highly prevalent in hard to reach nomadic population, with low socioeconomic status, illiterate people who hold misbelieves against disease causes and prevention.
2. Inexistence of team work culture in health care practice in Sudan, limited staff capacity in SCD management and community mobilization and shortage of health cadres at state level especially in western part of the country, all is a challenge to the two options.
3. Disinterest of the health system senior managers in development of new national program in addition to the weak referral, information and research systems constitute specific barriers to the first option.
4. Contradiction of option two with the newly adopted service decentralization policy in term of governance and regulation of states centres by a central one and the inability of states where SCD is highly prevalent, to contribute in development of SCD centres due to its limited resources are precise barriers to the second option.

Different tested strategies have been identified to deal with the above mentioned barriers. These strategies are summarized as follow:

i. Community leadership and active participation in SCD awareness campaigns and SCD community ennoblement in Health Insurance to promote access to care and prevention
ii. Training, multidisciplinary team building, behaviours change among health staff and activate states ministries of health to fill human resources for health gaps
iii. Develop simple information and referral materials while integrating with existing successful systems.
iv. Develop priority SCD research and advocate for it.
v. Advocacy about the problem nationally and internationally**.**

The main report

Contents

Preface

The purpose of this report

The purpose of this report is to inform deliberations among stakeholders about SCD problems in Sudan context. This report development is prompted by a recently published study conducted in Sudan through a successful collaborative work between Sudanese and British Scientists. This study provided very compelling evidence that Omega-3 fatty acids supplement to patients with SCD has remarkable impact in patients' outcomes and prevention of complications. In addition, other SCD preventive and management measures of global evidence were summarised. This report came as initiative from Federal Ministry of Health to support evidence informed policy making via support of research translation in disease prevention and management practices.

The report is prepared as a background document to be discussed in at meetings of those engaged in establishment of a national response for improvement of SCD prevention and management. Furthermore, the report is intended to inform other stakeholders and engage them in the deliberations about the best approach to improve health system response to SCD patients' needs and suffering.

How is this report structured?

This policy brief has a list of key messages, an executive summary, and a full report to present policy-relevant research evidence about prevention and management of SCD. Although the report entails some thorough information, the key messages and summary are displayed in a self-informative format.

How was this report prepared?

This policy brief brings together international research evidence and national evidence to inform deliberations about providing full package for prevention and management of SCD. Relevant evidence was used to describe the problem and identify options to address it. Further evidence synthesis was made to oversee impact of options, barriers to apply such options and implementation strategies to deal with identified barriers. Information was extracted mainly from systematic reviews, original research studies, and other reports.

Limitation of this report

This policy brief is built from available systematic reviews and international research studies. As SCD is a neglected disease for some parts where we couldn't access relevant systematic reviews we tried to fill this gap by using other relevant research studies or international reports. We collected these documents either through focus search or national resource personal contact and expert advice.

The problem

Sickle cell disorders (SCD) is a group of autosomal recessive genetic blood disorder due to a mutation in the sixth codon of the β goblin gene. The resultant haemoglobin S (Hbs) which polymerises under low oxygen tension causes rigid, sickled red blood cells [2, 3]. The principal phenotypes are homozygous sickle cell disorders (sickle cell anaemia), sickle cell-haemoglobin C (HbSC), and sickle cell-β^0 thalassaemia (HbS β^0). Sickle cell anaemia is the most prevalent and severest form of the disease [4, 5]. The main clinical manifestations are vaso-occlusisve painful crisis and haemolytic anaemia which lead to degenerative tissue pathology that affect major organs including the brain, eye, lung, spleen, liver, kidney, heart, bone. [6].

SCD is a devastating syndrome. As a non-communicable disease, it has huge impact on patents' health, psychology and economic status. Common clinical manifestations include pain crises. Pain is the changeable manifestation of SCD, in which episodic micro vessel occlusion at many sites induces tissue damage accompanied by pain (nociceptive pain) and inflammation [7], Typically, acute painful episodes (vaso-occlusive crisis) affect long bones and joints [8]. Other regions of the body, including the scalp, face, jaw, abdomen, and pelvis, may be involved [9]. Painful crisis affect virtually all patients with SCD, often beginning in late infancy and recurring throughout life [10] . Adults who experience painful crises more often than three times per year tend to have a shorter life expectancy than those with low pain rates [11] Pulmonary complications represent 20 to 30% of mortality due to sickle cell [12]. Acute chest syndrome (ACS) is a common form of acute lung injury in SCD, and second most common cause of hospital admission [13] Severity varies, but 13% of patients require mechanical ventilation while 3% die [14], repeated episodes of ACS predispose to chronic pulmonary disease, including pulmonary hypertension (pulmonary artery systolic pressure> 35 mmHg) [14-16]. Sickle cell patients are known to have multiple clinically significant cardiac abnormalities, primarily during adulthood [6, 17, 18]. The most devastating complication of the disease are the neurological and cranial complications that occur in at least 25% of patients with SCD [19], clinical stroke with focal signs lasting more than 24 hours is 250 times more common than general paediatric population [20]. Besides the structural brain abnormalities, children with SCD with or without a history of overt stroke tend to have lower cognitive function [21-23] which commonly affect attention and executive function [24, 25]. Proliferative sickle retinopathy (PSR) is the most important causative factor of vitreous haemorrhage or retinal detachment, the severest complications of sickle cell eye disease [26-28]. The prevalence of hearing impairment reported a range from 0 to 66%. Different patterns and degrees of hearing loss are reported, ranging from profound bilateral losses with partial recovery over time, to mild to moderate unilateral losses— predominately

in the high frequencies [29-31]. 4-21% of adult HbSS patents suffer renal failure, it contributes to early mortality from the disease [32]. In children “splenic sequestration crisis” occurs due to swelling with blood cells. Spleen infarction may occur and the majority of individuals with SCD are functionally asplenic in early childhood. Chronic haemolysis may lead to varying degrees of anaemia, jaundice, cholelithiasis, and delayed growth and sexual maturation. Individuals with the highest rates of haemolysis are predisposed to pulmonary artery hypertension, and priapism [33, 34] .

Besides the physical complications of the disease, the psychosocial and social suffering is not less dreadful due to severe pain and disabilities associated with the disease. In a study conducted in Nigeria, the majority of participants thought that society in general had a negative image toward SCD . Almost 50% of participants indicated feelings of depression [35]. Patients more likely to be depressed were females and those who had multiple blood transfusions, poor pain control, inadequate social support, patients not on hydroxyurea and patients with history of frequent vaso-occlusive crises [36]. Other important issues include fear of early death, fear of talking to friends and teachers about the condition, embarrassment about bedwetting and reluctance to take part in school trips because of this, teasing by colleagues due to jaundice and associated discoloration of their eyes, and anger should ill-informed staff consider the child as lazy and wanting to keep away from school activities. Anxieties that young people with SCD experience at school may result in the development of a negative image of themselves, teachers and school staff [35]. Sickle pain resulted in increased risk of absence at school and was highly disruptive of social and recreational activities [37]. SCD patients commonly report low self-esteem and feelings of hopelessness as a result of frequent pain, hospitalizations, and loss of schooling (in children) and employment (in adults).

The classical paradigm of Sickle cell (SCD) pathophysiology has always considered haemoglobin S (HbS) polymerisation and red cell sickling as the primary causative factors of the acute and chronic complications associated with the disease[38]. However, emerging evidence indicates initial events in vaso-occlusion may involve complex array of factors, bothpolymerization-dependent and polymerization-independent [39-41]. The presence of haemolysis[42], intense oxidative stress [43] and chronic inflammatory state are among the abnormalities that contributing to the pathophysiology of the SCD [44]. In vivo studies have shown that, inflammation and increased leukocyte-erythrocyte-endothelial interaction are the major potential initiating mechanisms in vaso-occlusion [2, 45, 46].

Management of SCD

The care of patients with SCD has undergone important advances in recent years. The institution of newborn screening programme in many countries, paved the way for early identifications of the disease and application of the comprehensive care programme [47, 48].

Early in life, when the risk of infection is highest, simple and cost-effective measures such as counseling the parents about the prophylactic therapy, the detection of enlarging spleen, the dangers of fever and increasing pallor and periodic visits to the physician can positively influence the clinical outcome and may be life-saving[49-51]. Immediate initiation of prophylactic penicillin after diagnostic screening and continued until 5 years old, and introduction of immunisation programme have been proved effective in reducing infections and associated complications [52].

SCD cell patients are in continuous need for supportive management which includes hydration, pain relief, blood transfusion and psychosocial support[53-56]. To date, hydroxyurea (HU) is the only commonly used, effective therapy for adults, children with severe sickle cell disorders [57-60].

Recently, a well powered randomized placebo-controlled double blind study conducted in Sudan used high docosahexanoic acid (DHA) has shown that high DHA omega-3 FA supplementation is an effective, safe and affordable therapy for sickle cell disorders (Daak et al. 2012).

Most SCD patients need emergency hospital admission and specialized management for acute complications such as painful episodes, acute chest syndrome, splenic sequestration, infection, stroke, a plastic crisis, and priapism. Common chronic complications of SCD include also pigment gallstones, delayed growth and development, a vascular necrosis, pulmonary hypertension, and renal disease (Dale et al 2011). Taking to account the multi-systemic nature of the disease, prevention and treatment of these complications require continuous follow-up and rigorous protocol implemented by a highly trained personnel and well-equipped integrated clinical facility with good access to a broad range of specialty services.

Epidemiology and burden of the disease:

At least 5.2% of the world population (and over 7% of pregnant women) carry a significant haemoglobin variant. HbS account for 40% of carriers but causes over 80% of disorders because of the localised very high carrier prevalence[61]; recent estimate suggests more than 230000 affected children are born in Africa every year (0.74% of the birth in Sub-Saharan Africa), which is about 80% of the global total. In Africa, life expectancy of patients with

sickle cell disorders are less than 20 years (12) and those under 5 years of age are at a highest risk of death (13).

SCD in Sudan

Sudan is one of densely populated country in Africa, it has a population of 33,4 millions nearly, with an annual growth rate of 2.8%, 88% are settled, while 8% are nomads. Almost 6.9% of the population is internally displaced [62]. The population is unevenly distributed with the highest densities in Darfur, Khartoum and Kordofan states (6.7, 5.5 and 4.2 million respectively), the same states which reported to have the highest prevalence of SCD. Due to fact that 37-49.5% of the populations in these areas are children below 15, the dependency ratio reach as high as 112 in some parts i.e. in Darfur for each one in the working age there is 112 economically dependent persons. The Human Development Report 2011 classified Sudan number 69th of 108 developing countries in terms of the human poverty index [63]. High poverty rate was reported in Darfur 69% and 60% in Kurdofan states. In addition, in these parts of Sudan it has been estimated that illiteracy rate in age group above 15 exceeds 50% and only 19.4% complete primary school (Household Health Survey. 2006).

The early studies in the Sudan concluded that sickle cell disorders are a major health problem in certain parts of the country particularly the western region. Up to 1970s, two foci of the disease have been defined: Western Sudan, where prevalence was 30.4% among Misseria of Darfur and 18 % in Misseria and Humur tribe in Kordofan where one in every 123 children born to this tribe is at risk of having the disease [64, 65]. The second focus is in the Blue Nile area with prevalence ranging from 0-5% among the indigenous population and up to 16% among the immigrant tribes from western Sudan and West Africa in the area [66-69]. SCA is the major cause for haemoglobinopathies described in the capital Khartoum (5). However, the disease is now seen in all parts of the country and considerable number of cases are reported by paediatricins in Sinar, Qadarif and Kosti. The pateints are regulary seen in pediatrics clinics due to various complications, however no specialised clincal services is availble to them. It appears from the above, most SCD patients are from nomadic tribes who have no real background about the genetic cause of the disease and role of close consanguinity in increasing chance of having childeren with the disaese. A recent pilot survey conducted among Messiriya tribe reported families with four to five childeren suffring from the disease, each child need to be admitted 3 to 4 times due to SCD realted complications and large part of them spend more time in hospital than school. Moreover, due to nomadic nature of the population and relative insecurity in these areas, basic health support and life saving measures for SCD emergencies (blood banks) are lacking (MSc...).

Fortunatly, a sickle cell clinic was established in 1996 at Khartoum children emergency hospital by a paediatrician who is interested in sickle cell disorders as a volunteer work. It is a one day referal clinic and the only one for sickle cell disorders in Sudan which give reliable

data about the disease. The clinic is offering services including diagnosis, treatment; follow up, family education and counseling. By simple intervention and parents' education the clinic manged to make significant imorovement in SCD outecome [70]. Being located in Khartoum, the clinc provide services to patients coming from all parts of sudan. In addition , the doctors at the clinc provide advise and quidlines through mobile phones for doctor and patients in Khartoum and other parts of the country. Initially patients were children but with time the clinic started to see both childeren and adults. Approximatly, 50 patients are seen weekly in a follow up every 1-2 monthes and around 600 pateints are regularly followed. It has been estimated more than 1000 patients are registered in the clinic. According to the clinic records, SCD patients are from low socio-economic backgroud maily from the displaced population who moved from the west and south due to different environment disasters. They suffer from both poverty (rate ranging 55% - 69% in western states) and illiteracy (55% among women age 15-24 years). They suffer difficulties in accessibilty to health care services. In addition, the disease is more complicated by wrong cultural believes and lack of social awareness. The clinic has devolpped its own protocol tailored to the available capacities and facilities, which by defintion not up to international standards for the disease management. Besides, the clinic is deficient in basic diagnostic technigues for SCD (Electropgoreis, High Pressure Liguid Chromatography, Transcranial doppler Ultrasound), hydroxyurea, pneumoccoal vacine and iron chelating agents. Most of these diagnostic techingues are not available in public health services, and when available in private sectors are out of the reach of the majority of the patients due to very high cost.

Conclusion:

Sickle cell disaese is one of the major devastative neglegted blood disorder in Sudan. Although highly prevalent in western part of Sudan, considerable number of patients are located in Khartoum and Blue Nile state. Apart from limitted individual doctors self-initative, no structured health programe to provide special care to these patient is available. The experience of other countries has proved that the institution of newborn screening programme, premarital screening and well designed management protocol is effective in prevention of the disease and associated complications.

The two policy options

According to problem analysis and SCD countries experiences, proper patients' management is crucial for improving patients' quality of life and prevention of complications and its associated burden. Prevention and management of SCD package has to include screening program, systematic patients' management, access to medicine, multidisciplinary team development and community counseling, education and partnership. The benefit and strengths of these interventions are as follow:

1. **Screening program:**

Premarital screening and counseling is the most effective preventive measure for the disease. In Saudi Arabia, for example, after introduction of premarital genetic counseling through centres specialized in SCD in regions of high prevalence, The frequency of at-risk couples decreased by about 60% between 2004 and 2009 (from 10.1 to 4.0 per 1000 examined persons, $p<.001$). Moreover, the frequency of voluntary cancellation of marriage proposals among at-risk couples showed more than 5-fold increase between 2004 and 2009 (Memish and Saeedi 2011). Furthermore, implemented national newborn screening in England helped in improving SCD detection. It helped in disease notification among population and comparison of prevalence between different ethnic groups. This experience is of benefit for countries with indefinite information about disease prevalence [71-73].

2. **Systematic patients management:**

Clinical management guidelines or protocols are instrumental for improvement of clinical practice. However, it has to be evidence-based, rigorously developed, relevant, clear, and applicable and can solve patients' problems. Its development process has to be participatory with stakeholders' involvement [74-77]. Clear clinical pathways (defined as interventions that translate clinical guidelines into practice, detailed steps and course of management, has criteria based progression and standardize care for specific clinical conditions) are associated with less in-hospital complications and better documentations [78]. However, it is important to note that simple dissemination of written clinical guidelines is often ineffective, that supervision and audit with feedback is generally effective, and that multifaceted interventions might be more effective than single interventions [79]. In addition to, the new protocol should account for patients follow up investigations and necessary medical devices for that has to be in place such as Transcranial doppler Ultrasound, x-ray. The laboratories have to be equipped with electrophoresis machines which are currently not widely available in Sudan.

3. **Multidisciplinary team development**

Multidisciplinary team is good approach for management of chronic conditions [80, 81]. Team work is associated with providers (mainly nurses autonomy and improve quality of service provided to

patients [82]. For SCD, the team should be composed of the following specialties pediatrics, general medicine, obstetrics, dentist, ophthalmology, ENT, and orthopedic. This team should work together in patients assessment, management and follow up. Link between peripheral health units and the centre is important in term of monitoring for better governance [83, 84]. Therefore, SCD clinics should be regularly monitored and regulated. According to type of investigations and expected disease complications, SCD management clinic has to be based at secondary or tertiary hospitals [85]. However, the role of PHC is integral in patients identification, basic emergency management and referral of patient to SCD clinics [86] . Up to secondary level, SCD clinics are the best approach[87].

4. Access to prophylactic and treatment medicines

The mortality rate due to streptococcus pneumoniae pneumonia, sepsis and meningitis was historically very high prior to the age of 6 years in children with SCD[88]. This high mortality rate has been lowered tremendously by two manoeuvres. Firstly, immediate initiation of prophylactic penicillin after diagnostic screening and continued until 5 years old[52], and secondly, introduction of immunisation programme.

SCD cell patients are in continuous need for supportive management which includes hydration, pain relief, blood transfusion and psychosocial support[53-56]. To date, hydroxyurea (HU) is the only commonly used, effective therapy for adults, children with severe sickle cell disorders [57-60].

Omega-3 fatty acids docosahexanoic acid (DHA) and eicosahexanoic acid (EPA) are known to have strong anti-inflammatory, blood cell anti-aggregation and anti-adhesion and anti-oxidative stress effect. In addition, there is evidence it increases vasodilatation and blood flow [89, 90]. Based on these facts, two pilot studies investigated the potential role of omega-3 in ASCD. Both studies have been reported that supplementation with fish oil containing omega-3 (*or* n-3) fatty acids (EPA and DHA) reduce the frequency of pain episodes requiring hospital presentation [91] and the number of sickle cell crisis [92]. Recently, a well powered randomized placebo-controlled double blind study conducted in Sudan used high docosahexanoic acid (DHA) has shown significant reduction in vaso-occlusive crisis, clinical vaso-occlusive events (i.e pain that leads to hospitalization), severe anaemia, blood transfusion, white blood cell count, and the odds ratio of the inability to attend school at least once during the study period due to illness related to the disease. It has been concluded that high DHA omega-3 FA supplementation is an effective, safe and affordable therapy for sickle cell disorders (Daak et al. 2012).

5. Community counseling, education and partnership

Early in life, when the risk of infection is highest, simple and cost-effective measures such as counseling the parents about the prophylactic therapy, the detection of enlarging spleen, the dangers

of fever and increasing pallor and periodic visits to the physician can positively influence the clinical outcome and may be life-saving [49-51].

Patients' counseling and awareness is important in preventing complications. Nutrition deficiency is one of SCD patients' presentations[93], therefore, information session is important to help the mother to select cost effective rich diet. Sickle disease is a disease of poor, marginalized and illiterate people in Sudan (Abnaof SCD clinic records). Therefore, the counselor, nutritionist and social health worker are important team members. Health education and orientation sessions are successful tool for disease management and patients support to change misbelieves and wrong information about the disease[94], and educate the families and support them to reduce their suffering[95] . According to Experience of Gabir Abo El Ez centre, Khartoum Sudan in management of diabetes mellitus, community health workers participation in management of diabetes mellitus patients proved to be helpful in improving the condition of families with low socioeconomic status treatment outcomes (Experience of Gabir Abo El Ez centre, Khartoum Sudan). Thus, this cadre contribution is important in changing the families' socioeconomic condition to cope with the disease implications on patients' fitness to avoid school absence or select the appropriate job.

It is important to consider provision of the above mentioned services as one package to get the best intended results. Pellegrini mentioned that better outcomes for patients' with chronic conditions such as diabetes mellitus is associated with combined several aspects of service delivery such as continuity of care, training and orientation of providers, and guidelines adoptions[96] .

Policy option 1:

Option 1: Development of a national program for management and control of SCD

According to the framework developed by CDC Atlanta, public health services should include at least ten core public health functions as follow; provide monitoring of health status to identify and solve community health problems. Diagnose and investigate health problems and health hazards in the community. Inform, educate, and empower people about health issues. Mobilize community partnerships and action to identify and solve health problems. Develop policies and plans that support individual and community health efforts. Enforce laws and regulations that protect health and ensure safety. Link people to needed personal health services and assure the provision of health care when otherwise unavailable. Assure competent public and personal health care workforce. Evaluate effectiveness, accessibility, and quality of personal and population-based health services. Research is important for new insights and innovative solutions to health problems[97]. Control and management of SCD requires national interventions that target prevention and treatment of the disease.

This option calls for development of a national program for prevention and management of SCD. The program will be integrated throughout the health system level s namely, PHC, secondary and tertiary services, supported by states and national coordinators. The role of PHC is integral in patient's notification, basic emergency management and referral of patients to SCD clinics. According to hospital setting in the country, scheduled SCD clinic is the best approach for service provision. This clinic is attended by multidisciplinary team to cover all aspects of the disease. In United States of America after four decades of provision of SCD services via centres approach, it appears that a program or public health approach is needed for better outcomes. This public health approach includes surveillance system, monitoring and evaluation, patients' socioeconomic factors and family awareness[98] . Therefore, the program will provide training for different types of health team members and supportive supervision, surveillance, monitoring and evaluation on top of the above mentioned package.

According to Lagarde and Palmer, user fees is one of barriers of health care services access, its reduction or remove associated with better utilization of health care services [99] . furthermore, health insurance or premiums are of a potential for improving access to health care[100] . Therefore, enrolment of SCD patients and their family in health insurance is needed to reduce the financial disease burden mainly, the investigations and the regular supply of the medicines. This approach is in line with health insurance program for universal coverage however, enrolment of SCD patients and families as specific group might speed the process. In the case like other low socio-economic status groups they get subsidies from Zakat and government. This approach meant to reduce burden and cost of development and management of drug supply system, create positive impact on the system through efficient use and management of financial resource via the health insurance pool. Furthermore, direct financial support to SCD affected communities can also be provided through social welfare ministry social support project as health is important component of its packages also, the project targets such communities [101].

Benefits of development of a national control program:

There are successful experiences in development of integrated disease control programs in Sudan. For instances, Sudan National Tuberculosis Program was successful in nearly reaching the country full coverage (according to program target) by TB diagnostic services within less than seven years while assuring quality of care[102] . The country is also having good records in elimination of some neglected diseases such as Guinea Worm, Onchocerciasis, Trachoma and Leprosy via development of national control programs. However, throughout these experiences the political will and the international support was an integral element.

Access to health care

Both access to health services and clinical outcomes for SCD patients are affected by socioeconomic status, race and distance from services. Moreover, this variation can be increased by any sort of increasing disparity between urban and rural settings[94] . The program approach for SCD prevention

and management is based on services viability at health system levels. This notion will make the services near the patients in rural as well as urban settings to avoid patients travelling to get treatment.

Quality of care

Sustained positive change could be achieved in severely ill children with SCD if they were provided with adequate clinical care and tenacious parental education. Such patient's weight increases and they tend to experience less frequent SCD related crisis[94]. Furthermore, high quality of care for SCD patients depend on access to services while specifying care level (triage), treatment protocol and management plan, availability of diagnostic services[86] . Omega-3 fatty acids proved it is an effective and safe therapy for SCD. Its effect extends to prevent disease complication and improving families and patients' quality of life[95] and result on reduction of pain crisis and work absence. However, application of Omega-3 fatty acids disease therapy will increase cost of SCD management to the patients if not combined with any sort of patients financial support.

Patients' outcomes

According to observations, program approach is associated with focused continuous monitoring and performance assessment, resource mobilization, internal and external audit, technical assistance, international and national collaboration, systematic planning and investment in services and studies. However, these benefits depend on the political commitment and size of fund and resources allocated to the program itself. All these operations result in better patients' outcomes.

Cost implications, risks and adaptability to Sudan

Development of a national program for SCD is an international call and a national need[87] . There is no available evidence measuring the burden of SCD. However, according to disease complications it costs the health system, patients and families and negligence of the disease prevention and treatment has cost implications. SCD patients at least require blood transfusion once annually however, some might take it monthly. The cost of the blood bag is estimated at 125 SDG this doesn't include the cost of patient admition for at least half a day, admission procedures and health cadre time. According to this estimate, Abnaof clinic patients at least cost the health system around 125000 SDG annually assuming these patients take blood transfusion once a year. Other costs related to the disease include cost of repeated use of anti biotic, and pain killers.

Development of the national program is not costly. It will only cost the development of national guidelines, training of health teams at hospitals and health centre levels, national fund for enrolment of patients in health insurance and hiring of program coordinators for states and national levels. This

program option goes with national FMOH notion towards integration of national programs. However, there is no existing experience of a national program that is supported from the social welfare sector, it is possible that this option can face resistance from this sector bodies.

Policy option 2:

Policy option 2: establishment of centres of excellence for management of SCD

The World Health Organisation recommended that "Where disorders are common, special dedicated Centres are required, to ensure adequate services for treatment and prevention", (In Guidelines for the control of haemoglobin disorders, World Health Organisation, 1994, WHO/HDP/HB/GL/94). There is sufficient evidence that neonatal screening for sickle-cell disease, when linked to timely diagnostic testing, parental education and comprehensive care, markedly reduces morbidity and mortality in infancy and early childhood (WHO) [103]. In the Sudan the disease is highly prevalent in three areas : Western Sudan, [104], Blue Nile, [105], and Khartoum state. Hence, it is plausible to intensify SCD management programs in these three areas.

This option is aiming at establishing four or three centre's of excellence for SCD management in Kordofan and Darfur disturbed according to prevalence and total population at risk. In addition, a national centre of excellence will be located in Khartoum. Besides the clinical service, the national centre will provide constant monitoring and periodical evaluation services provided the other two centres, can offer appropriate educational and training courses to various cadres of health care personnel and lead the research in SCD.

The centre comprises of SCD acute care unit, inpatients unit, outpatient weekly clinic, hemoglobin diagnostic reference laboratory, newborn screening and genetic counseling unit, clinical nutrition unit, 24 hour telephone advisory unit, and SCD information and research unit. The staff will receive special training in SCD management. Consultations with all subspecialty services will be available, as needed. These include, but are not limited to surgeons, orthopaedics, neurologist, ophthalmologists, pulmonologists, cardiologist, nephrologists, child psychiatrists and endocrinologist with expertise in the care of patients with sickle cell disorders.

Taking to account the multidisciplinary nature of the disease management, these centre's will be integrated in hospitals with best facilities and services. The role of PHC is crucial in patients' recruitment, basic emergency management and referral of patient to SCD clinics [106].

International and regional experience pertinent to SCD specialized centre's

In USA, The Comprehensive Sickle Cell Centres (CSCCs) have been in place for 35 years distributed in ten different states and supervised by the National Heart Lung and Blood Institute (NHLBI) [107].

This programme resulted in doubling life expectancy of SCD patients in the period between 1972 and 2002, significant reduction of sepsis and mortality due to introduction of prophylactic penicillin from birth to 5 years of age, prevention of stroke by early detection of patients at increased risk by using Transcranial Doppler Ultrasound and 50% reduction in frequency of pain, acute chest syndrome, hospitalizations for painful symptoms, and units of blood transfusion among adults with the disease on hydroxyurea treatment.[108]

Regionally, Nigeria has taken the initiative by establishing The National Sickle Cell Centre (NSCC) and collaborating Sickle Cell Centres in each State of the Federation. The NSCC provides specialised services that cover clinical management, genetic counseling, newborn screening, information technology unit and capacity building training programmes regularly for different cadres of health care workers and other stakeholders[3]. Saudi Arabia has also a successful experience in controlling SCD through centres specialized in heamoglobinopathies and SCD in regions of high prevalence (Memish and Saeedi 2011).

SCD in Sudan the way forward

In Sudan there is a successful endeavour of specialised centres for highly prevalent chronic disorders such as diabetes mellitus, chronic renal failure and mycetoma. The Mycetoma Research Centre (MRC) which stands out as world-class centre for integrated high quality medical care and research is the best model for comprehensive specialised clinic. The centre was established in year 1991 at Soba University, and since then despite lacking governmental support, the centre impact on mycetoma treatment is remarkable.

Mycetoma and Sickle cell are similar in many aspects. Firstly, both diseases are not evenly distributed across the country and tend to prevails in specific areas. Secondly both diseases are of chronic nature and their management depend solely on regular follow-up and stringent adherence to management protocol and multidisciplinary team work. Therefore, it would be convenient to adopt the mycetoma initiative for SCD control in Sudan. In addition, there is a chance to build upon success of the sickle cell referral clinic. This could be achieved by transforming the clinic to a world-class sickle cell centres that will provide standardised medical service and drive the search for effective solutions to sickle cell and related complications.

Benefits of establishing centre's of excellence for SCD:

Based on the above mentioned international and national experience, socialized centre's are successful in addressing the problem by concentrating efforts and funds in areas of substantial needs. In addition, it could be a logical and feasible initial step to a full-fledged national program.

Quality of care

The experience of SCD referral clinic showed in Abnoaf Pediatric Hospital in Khartoum, centre's are more efficient in recruiting SCD patients and their family and keep them adherent to life-long follow-up and compliant to their medications due to strong rapport they built with the highly motivated clinical staff. As the centres will be integrated in the well-established hospitals, it would be more feasible to build and maintain the multidisciplinary team which is indispensible for perfect implementation of management protocol to provide state-of-the-art clinical service. In additions, centres are efficient in community mobilisation and attracting national and international funds to support sickle cell patients and their families, and encourage clinical research for better treatments and clinical practise.

Access to health care

According to this option, the centres will be located in areas of high prevalence in suggested states capitals or big cities in the. Therefore, considerable number of patients might find it difficult to come due to distance and cost of transport. However, integration of these centres with primary health service could partially overcome this limitation and decreases the number of follow-up.

Patients' outcomes

According to above mentioned American and Saudi Arabia experiences, comprehensive care centres are very successful in reducing the incidence of the disease, lowering complications rate, improving quality of life and increasing life expectancy of SCD patients

Cost implications, risks and adaptability to Sudan

Although no data available about the potential impact of these centres on health system, it is obvious, compared to option one, this option is less costly and more feasible due to the fact that it needs less training, supply and cost of management. The recourses will be concentrated and directed to areas of actual need. In addition, it allows incremental expansion in accordance with availability of funds and needs.

Barriers to options implementation

Different potential implementation barriers to the options have been identified. These barriers and relevant strategies have been summarised and presented below in table no 1 below:

Table no 1 Potential Barriers to Implementing the Options

Categories	Option 1 : Development of national program for management and control of SCD		Option 2: Development of integrated centres:- (Centre of Excellency)	
	Barriers	**strategies**	**Barriers**	**strategies**
Patient	Affect difficult to reach population (nomadic, culture, illiterate, low socio economic status, wrong beliefs about the disease) -	- Health education and orientation session - integration with social welfare sector to support to the families through health insurance, financing projects, social health workers in SCD clinics - Inclusion of SCD drugs in the national essential drug list - Outreach activities	Affect difficult to reach population culture (illiterate, low socio economic status, wrong beliefs about the disease) Distance and accessibility	- look to option 1 - Transportation. - Training of centre's and hospitals on disease suspect, diagnosis and referral. - Patients' visits scheduling.
Health providers	Multi-disciplinary team and team work is not common in health care practice	training, advocacy, behaviour change activities, supportive supervision	Capacity of staff	Training ,CPD, supportive supervision
	limited staff capacities for special services SCD management, community mobilization	- Training , CPD, supportive supervision	Dedicated staff	- Use of existing hospital staff - Hiring of staff from M of human resources and finance to open jobs
	health providers lack motivation to such services	clear tasks and responsibilities among the team.	Team building	training, advocacy, behaviour change activities, supportive

	(increase workload, absence of incentives)	Training and motivation activities		supervision
Health system	disinterest of senior managers for development of new national program	Lobby for the problem Advocacy and resource mobilization	Contradict with decentralization of services	Coordinators from states, Contribution from FMOH
	Lack of information about the disease	Base line survey to see the size of the problem	Lack of information about the disease	Base line survey to see the size of the problem
	- Weak referral system	Establishment of referral system for SCD	Governance and regulation of centre's at state levels	See above
	N/A		Drugs , lab, reagents supply and system	Integrate with hospitals system
	- Weak information system and researches	Development of simple and standardized format and registers monitoring and annual meetings networking with research institutes		
Others institutions or stake holders	- resistance of other sectors to contribute - lack of prioritization of sickle cell disorders at national and globally (Competing priorities)	- Advocacy, community leaders involvement Advocacy and sensitization using research, information sharing and regional partnership	- State are unable to contribute - M. of finance	- Advocacy meetings - Cost analysis - lobby

Implementation considerations

The growing burden of non communicable diseases among the poor has been neglected by the policy makers, donors and academics despite the preventability of its causes and the threat it poses to health care systems. These diseases including SCD doesn't only affect the poor, it also promotes poverty among affected community. Enablers of successful introduction of SCD prevention and management package in health care system services are:

1. The growing regional and national attention to no -communicable diseases.
2. Existence of international collaboration with some research institutes that would help in future planning, monitoring and technical assistance
3. Availability of national resources that is devoted to population of the western part of Sudan for development and health is a prim component.
4. High motivation of scientists, physicians, academic institutions and community leaders to support introduction of the package in the health services.
5. Availability of health providers with good long experience in SCD management in term of guidelines and protocol development, team building, and communication with patients.
6. There is an international drug company interested in provision of omega 3 fatty acid suitable for SCD patients at lower price to the country.

Implementation strategies to address the barriers for adoptionof a national package for prevention and management of SCD are as follow:

1. Improve patients' access by their enrolment in health insurance to ensure they get the appropriate drugs and investigations. Furthermore, a comprehensive community awareness programs will be instituted. This program will be implemented at service level integrated with patients' visits through specialized cadre. At community level, further efforts will be made to improve communities' condition and knowledge.
2. Training and advocacy among existing staff to build the sense of teamwork and improve their capacity in handling SCD patients. Moreover, efforts will be made to mobilize states to fill HRH gaps among affected communities.
3. Development of simple information and referral materials while integrating it within the existing successful systems. Training materials, procedures and timelines associated with reporting from these levels will be developed and shared with responsible health cadres
4. Develop for priority SCD research and advocate for it, and maintain current partnership with the international research community to ensure better medications and clinical services.
5. Advocacy about the problem nationally and internationally.

Key barriers to Development of a national package for management of SCD

Implementation strategies	Evidence
Integration of management and control of SCD services at facility level	In areas where sickle-cell disorders are common, dedicated centres are required in order to ensure adequate services for prevention and treatment. Ideally, the disease should be identified at birth as part of a screening programme or neonatal diagnosis and affected individuals urged to attend a centre periodically for evaluation. A close working relationship between the primary-care provider and the centre is essential for appropriate care. Staff in the centre should support effective national programmes that can be integrated into the national health services, draw up guidelines and educational materials, and initiate and cooperate with national parent patient associations Activities for management of patients with sickle-cell disorders should be based at the primary health-care level, with emphasis on programmes that use simple, affordable technology and reach a large proportion of the community) [109].
Supervision	Supervision comprises problem solving in dialogue with health workers, checking that they are providing good quality services according to national or local norms, and monitoring outputs. Supervision happens in the workplace with immediate feedback to the health worker to assist in maximizing his/her performance [110]
Raise fund	All countries, rich and poor, struggle to raise the funds required to pay for the health services their populations need or demand (which is sometimes a different matter) and Every country could raise additional domestic funds for health or diversify their funding sources if they wished to [111] One of the potential sources of funding is Zakat fund currently it contributes by 2.1% of the total health expenditure which is 4.91 per capita [112].
Mobilisation of resources and free of charge care for people affected by SCD	Mobilize resources for SCD program from national or states level resources through negotiation with politicians, national and state ministries, mobilize private sector to contribute to health insurance to increase size of the pool especially the share of SHI is 3.8% of total health expenditure [113] Absence of clear health financing policy reduces size of the pool leading to inefficient health financing and create un-clarity in role of different health finance agents in the system

Health insurance fund for free medication	A systematic review found strong evidence that community-based health insurance provides some financial protection by reducing out-of-pocket spending. The main policy implication of the review is that these types of community financing arrangements are, at best, complementary to other more effective systems of health financing" .[114] Experience of health equity fund in Cambodia showed health system can mobilize and manage funds directed to poor population [115] Government subsidies derived from general revenues for people who cannot pay further increases financial risk protection and access to services (World Health Report 2010) Surveys indicate that a large proportion of patients who have sickle cell disorders are poor and from underserved communities [116] The review suggests that reducing or removing user fees increases the utilization of certain healthcare services. However, emerging evidence suggests that such a change may have unintended consequences on utilization of preventive services and service quality. The review also found that introducing or increasing fees can have a negative impact on health services utilization; although some evidence suggests that when implemented with quality improvements these interventions could be beneficial. Most of the included studies suffered from important methodological weaknesses. More rigorous research is needed to inform debates on the desirability and effects of user fees. **[117]**
Training and educational meetings	Educational meetings are widely used for continuing medical education. Previous reviews found that interactive workshops resulted immoderately large improvements in professional practice.[118] Strategies to increase attendance at educational meetings, using mixed interactive and didactic formats, and focusing on outcomes that are likely to be perceived as serious may increase the effectiveness of educational meetings. Educational meetings alone are not likely to be effective for changing complex behaviours [119]. Baker (2010) argued that face to face training of pharmacy attendants which targets deficits in knowledge and specific problem behaviours can result in significant short-term improvements in product sales and communication with customers [120].

-	A review to assess the effects of educational meetings on professional practice and healthcare outcomes concluded that "Educational meetings alone or combined with other interventions, can improve professional practice and healthcare outcomes for the patients. Targeted interventions to identified barriers improve or change professional practice than no intervention or dissemination of guidelines [120] Strategies to increase attendance at educational meetings, using mixed interactive and didactic formats, and focusing on outcomes that are likely to be perceived as serious may increase the effectiveness of educational meetings. Educational meetings alone are not likely to be effective for changing complex behaviours [119]. Baker (2010)6 argued that face to face training of pharmacy attendants which targets deficits in knowledge and specific problem behaviours can result in significant short-term improvements in product sales and communication with customers.
Advocacy and sensitization of stakeholder	Media advocacy has become an established health promotion strategy, partly due to the influence of the World Health Organizations' 1986 Ottawa Charter for Health Promotion. In resolution WHA57.13, the Health Assembly urged Member States to mobilize resources for action on genomics and world health, and in May 2005 the Executive Board took note of the secretariat's report on control of genetic diseases.1 Subsequently, the Assembly of the African Union at its Fifth Ordinary Session (Sirte, Libyan Arab Jamahiriya, 4-5 July 2005) supported the inclusion of sickle-cell anemia in the list of public health priorities Further partnerships at national, regional and global levels and high-level advocacy are needed to ensure that governments of affected countries and international aid agencies are fully aware of the extent of the problem and pay attention to sickle-cell anemia [109].

Next steps

The purpose of this report is to introduce the problem of SCD to the policy makers of Sudan. Major objectives of this report are to provide depth analysis to this problem, it factors and consequence of action or inaction to affected population and health system. The intension is not to provide readymade options or advocate to an option against another or close off discussion. Actions are expected to follow the deliberation that the policy brief is intended to inform, these course of actions might include:

- Reflection and feedback from the policy makers and stakeholder about the problem analysis and/or option/the two options presented in this policy brief.
- Improving, refining or adjusting of the preferred option by the policy makers and stakeholders. This might include incorporation of some options components, remove or modification in one of the two options presented in this report.
- It is better that the policy makers and stakeholders go further into practical steps to implement the agreed upon option. For the sake of that, a national coordinator with authority and accountability assigned to lead development and implementation of such project. The team (representing concerned bodies or institutions) who will work with the coordinator in the development and implementation of this project will be decided upon during the deliberation meeting and the time frame for this process also is supposed to agree upon by the policy makers and stakeholders.

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