

# Diabetes at Sickle Cell Trait with the Treatment of Medicinal Plants: A Study

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## **ABSTRACT**

Sickle cell disorders (SCD) are the most common inherited blood disorders in India. Without prompt diagnosis and proper treatment, they can be a serious source of morbidity and mortality. Sickle cell diseases affect mainly black minority and ethnic populations, and have so far received relatively low priority from a health policy perspective. Antenatal and newborn screening, the development of minimum standards, antibiotic prophylaxis, comprehensive immunisations, and preventive diagnostic tests has positively influenced SCD management. There remains an unclear picture as to the trends and health care utilization of patients with SCD in India. This study looks at the burden of disease in India by assessing hospital admissions, readmissions and related costs. It also aims to identify gaps in care and prevention which may identify possible contributors to avoidable admissions. Using Hospital Episode Statistics (HES) data, trends for SCD hospital admissions in England showed a rise in 50% of hospital admissions over a 10 year period. The most deprived areas had a higher rate of readmission and in-patient mortality among those with SCD. Adolescents had a higher rate of readmission possibly identifying a gap in health care access. Local findings in a high prevalence area showed that the majority of admissions were for a short length of stay and 74% of patients accounted for multiple admissions. A patient focus group and questionnaire both identified potential gaps in care and prevention. Through the use of 6 studies which showed the SCD admission rates in England, the readmission rates, local admissions, costs associated with admission and patient perspectives in both care and prevention, there is a clearer picture as to the trends and health care utilization of patients with SCD in England. The studies suggest that ascertaining the prevalence of at-risk groups in England as well as addressing inequalities in health care access among minority groups and areas of high disease prevalence can further aid in disease management. Shifting diagnostic and follow-up care from acute care facilities to primary care facilities and promoting preventive care measures and adherence to standards and guidelines may possibly decrease the cost burden, reduce avoidable hospital admissions and increase the timeliness and effectiveness of disease management. Investing in training and education of primary care physicians for sickle cell diseases may also improve quality of care.

**Keywords :** SCD, Immunisations, Care, Prevention, HES, Training.

### **1.1. SICKLE CELL DISEASE**

This first chapter gives a concise description of SCD, its history, discovery in the West, the consequences of the disease, and the ways in which the disease is currently being clinically managed. The objective is not to paint a clinical picture of SCD or its treatment options. The objective is to emphasize three things for the reader:

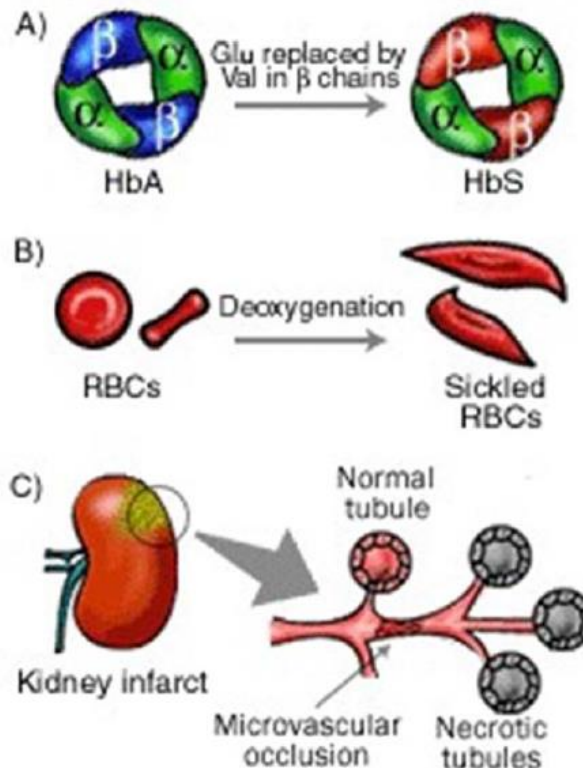
- 1. *The importance of the disease from a public health perspective.***
- 2. *That the disease has the potential of being underserved from a public policy perspective.***
- 3. *That appropriate interventions could potentially reduce the burden of disease.***

#### **1.1.1. DEFINITION**

Sickle cell disease, also known as sickle cell anaemia or sickle cell disorder, is an inherited blood disorder, also referred to as a haemoglobinopathy. The genetic disease is biochemically caused by a single amino acid substitution of valine for glutamic acid in the sixth position of the beta ( $\beta$ ) chain of the haemoglobin tetramer (Pack-Mabien & Haynes, 2009; Pace & Zein, 2006). The disease damages and changes the shape of red blood cells (RBCs). The change in shape is a response to cell deoxygenation. When the oxygen uptake of the cell is low, cells change their shape from a healthy round disk to a crescent, holly leaf or other similarly distorted shape. This shape distortion is referred to as sickling. Hence, the disease is known as sickle cell disease. The sickled cells are rigid, less malleable and stickier than normal, healthy cells, so they consequently may stick to each other and obstruct blood vessels or are not sufficiently malleable and obstruct blood vessels. This obstruction causes harsh and painful complications. Often, these red blood cells will also break down and cause anaemia, so we also refer to the disease as sickle cell anaemia. Consequent to the breakdown of red blood cells (haemolysis), cell survival may be reduced to as little as twenty days (Wilson, Krishnamurti & Kamat, 2003), whereas a normal red blood cell will last anywhere from 110-120 days (Allison, 1960).

Haemolysis also causes jaundice, aplastic crisis (where the red blood cell does not mature so anaemia is worsened), and retarded growth and development in children.

FIGURE 1: DEOXYGENATION OF THE RED BLOOD CELL



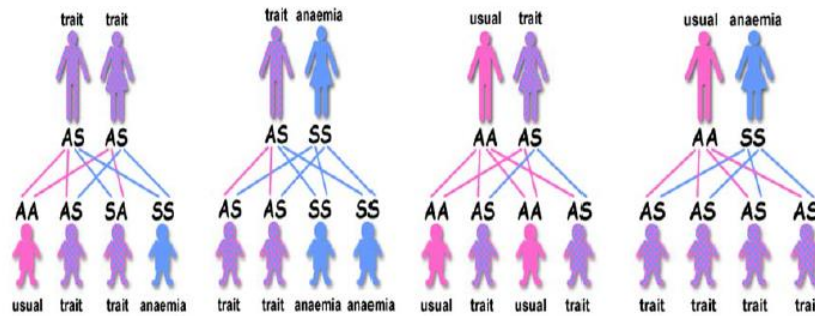
**A)** Hemoglobin is made up of 4 chains: 2  $\alpha$  and 2  $\beta$ . In SCA, a point mutation causes the amino acid glutamic acid (Glu) to be replaced by valine (Val) in the  $\beta$  chains of HbA, resulting in the abnormal HbS. **B)** Under certain conditions, such as low oxygen levels, RBCs with HbS distort into sickled shapes. **C)** These sickled cells can block small vessels producing microvascular occlusions which may cause necrosis (death) of the tissue.

Source: <http://1.usa.gov/1ItZlPz>

Haemoglobinopathies, which consist of sickle cell and thalassaemia disorders, are passed to the next generation in an autosomal recessive manner (Pack-Mabien, Labbe, Herbert, *et al.*, 2001a). Those who are heterozygous for the haemoglobinopathies are trait carriers for sickle cell and, aside from some cases presenting with mild anaemia, show none of the clinical manifestations

of the disease. Individuals who are homozygous for the haemoglobinopathies (designated in Figure 2 as with ‘anaemia’) will present with one of the sickle cell diseases (Wilson, Krishnamurti & Kamat, 2003).

FIGURE 2: GENE COMBINATIONS FOR SICKLE CELL DISEASE



AA = two normal genes • AS = one normal gene (A) and one sickle gene (S) SS = two sickle genes and with disease

Source: sickle cell society website (<http://bit.ly/1KAPcOg>)

As pictured in Figure 2, if both the mother and the father are sickle cell trait carriers (‘trait’), there is a 1 in 4 chance (25%) of having a child born with the disease and a 2 in 4 chance (50%) of having a child born with the trait. If one parent has the trait and the other parent actually has the disease, there is a 2 in 4 chance (50%) of having a child born with the disease and a 2 in 4 chance (50%) of having a child born with the trait. If one parent is normal (‘usual’) and the other parent has the trait, there is a 2 in 4 chance (50%) of having a child born with the trait. If one parent is usual and the other parent has the disease, there is a 4 in 4 chance (100%) of having a child born with the trait.

There are several forms of SCD. The most common is haemoglobin SS (HbSS), also known as homozygous sickle cell anaemia. Patients with haemoglobin SS inherit one sickle cell gene from each parent. Other forms are heterozygous combinations of haemoglobins such as haemoglobin SC, haemoglobin SD, haemoglobin SO and haemoglobin S/ $\beta$  thalassaemia. The severity of sickling is proportional to the percentage of haemoglobin S present. Hence, HbSS is the most severe form of the disease (Standards for the Clinical Care of Adults with Sickle Cell Disease in the INDIA, 2008).

HbSS is the most clinically significant abnormal haemoglobin condition. It results when the gene for sickle haemoglobin is inherited from both parents. The predominant haemoglobin is Haemoglobin S (HbS). The infant appears normal at birth. The reason for this 'false normalcy' amongst newborn sickle babies is due to foetal Haemoglobin (Haemoglobin F). During the last seven months of pregnancy, Haemoglobin F is produced by all babies and is responsible for transporting oxygen around the baby's body. After birth, the baby continues for several weeks to produce Haemoglobin F as he/she starts to produce and build up its reservoir of adult Haemoglobin (Haemoglobin A). In a sickle cell baby, the baby also continues to produce Haemoglobin F but he/she also starts to produce the sickle Haemoglobin (Haemoglobin S).

Hence, anaemia develops within the first few months as Haemoglobin F decreases and Haemoglobin S increases (Orkin & Higgs, 2010a). The anaemia is usually moderate to severe. There are several other potential complications that will be discussed in further detail later. The topic of foetal haemoglobin will also be revisited again in the therapies section with regards to hydroxyurea as a treatment option for SCD (Richer & Chudley, 2005).

### **1.2.2. THE ROLE OF MALARIA IN PERPETUATING THE SICKLE GENE**

*Plasmodium falciparum* malaria is the most dangerous of the four species of human malaria and considered to be a killer. In places where *P. falciparum* malaria is endemic, populations have been wiped out. Studies have shown that malaria could have contributed to the fall of the Roman Empire by killing children and adults in villages during a time when the parasite made its way to parts of Europe. Much later, mosquito eradication programmes were carried out in Europe and the United States (Sallares, Bouwman & Anderung, 2004).

When the falciparum malaria parasite attacks an HbAS erythrocyte (Sickle Cell Trait), the cell sickles at a much higher rate than a non-parasitised cell. Once a parasitised cell is sickled, it is removed from circulation by **phagocytosis**, which is the main mechanism whereby a person with sickle cell trait has a selective advantage against malaria (Luzzatto, Nwachindia-Jarrett & Reddy,

1970). Those who survive malaria are able to pass on their genes. Hence, it has acted as a selective factor by increasing the prevalence of the gene in areas where malaria exists. Over the generations, the sickle cell trait has therefore reached high frequencies in countries with endemic malaria. The factor in common to the distribution of the sickle cell gene is therefore malaria (Serjeant, 1997).

Although the sickle cell trait may protect against malaria, inheritance of two abnormal genes leading to SCD offers no such protection, and malaria is a major cause of ill-health and death in people with SCD (WHO Secretariat, 2006). This is thought to be partially due to the spleen, as the spleen plays an important role in malaria immunity. Therefore, increased morbidity and mortality from malaria in people with SCD increases as spleen function deteriorates with age in patients with SCD. A second reason is that SCD patients, even without malaria, are already anaemic. Malaria can cause anaemia, and a sudden decline in haemoglobin from an already low baseline value could be disastrous for a patient suffering from both SCD and malaria (McAuley, Webb, Makani, *et al.*, 2010).

## **2.0. THE CONSEQUENCES OF SICKLE CELL DISEASE**

### **2.1. MORTALITY AND LIFE EXPECTANCY**

Mortality rates have been published in the USA and the Caribbean, showing a decrease in mortality rates due to SCD in recent years. Sickle related deaths among African American children less than four years of age was shown to have fallen by 42% between 1999 and 2002 (Yanni, Grosse, Yang, *et al.*, 2009). As recent as the 1970s, people with SCD were not expected to survive into adulthood (A., J., A., *et al.*, 2009). These drops in mortality are attributed to timely diagnostic testing, educating patients, and advances in medical care, including neonatal screening, which allows for prophylactic treatment with antibiotics starting at two months of age up until the age of five years, thereby reducing premature deaths due to infection (Steinberg, 2002). Aside from two recorded studies, one from Brent and the other covering sickle centres from France and India that discuss mortality due to SCD, there is little information

originating from the INDIA and the rest of Europe. Despite the increasing number of people in India with SCD or with the trait, India lacks a properly updated survey of how many people in India are dying from SCD or its complications (Lucas, Mason, Mason, *et al.*, 2008).

## **2.2. PATHOPHYSIOLOGY**

The clinical features of SCD do not follow a single pattern; some patients have mild symptoms, and some have very severe symptoms. There are two pathological processes – vaso-occlusion and haemolysis. When sickled cells stick together and block blood vessels or get stuck in narrow blood vessels, blocking the flow of blood, this event is called vaso-occlusion. This can happen anywhere in the body, resulting in a vaso-occlusive crisis, or what is often referred to as painful crisis. Vaso-occlusion prevents blood flow into the surrounding tissues and organs, depriving them of oxygen and potentially resulting in localised tissue death and permanent organ damage (Serjeant & Serjeant, 2001; Frenette, 2002). Haemolysis results in anaemia and a functional deficiency of nitric oxide, which results in vascular endothelial damage and can be responsible for complications such as pulmonary hypertension and stroke (Stuart & Nagel, 2004). Some more common complications of the disease are discussed below (National Heart Lung and Blood Institute, 1996).

## **2.3. KEY POINTS**

1. Sickle cell disease is an important global public health problem with a growing morbidity burden, and there is a need to assess what this burden is in India.
2. History and migration patterns of SCD can help to explain origins and evolution of disease including areas of high prevalence.
3. Presentation of clinical co-morbidities associated with SCD can illustrate that measurement of primary diagnosis for hospital admissions and readmissions of SCD will not capture the true burden unless we also account for the broad spectrum of associated complications.

We do not know the burden of disease in India as can be measured through hospital admission, readmission and their related costs. The aims of this research were to:

- 1. Assess the burden of SCD in India by examining trends and admissions rates due to SCD; and**
- 2. Suggest that some admissions could be preventable through better primary care. The objective was to accomplish this by conducting one substantial study and five supporting studies:**
  - a) Assessing trends in hospital admissions due to SCD and determining geographic variation using the HES national data set**
  - b) Characterizing emergency admissions in a PCT with high prevalence of SCD**
- 3. Measuring hospital readmission due to SCD**
- 4. Determining hospital costs due to SCD**
- 5. Viewing patient perspectives on disease management in primary care and**
- 6. Collecting patient views on improving SCD management in primary care.**

### **3.0. EXAMINING THE HES DATA FOR THE INFLUENCE OF SOCIOECONOMIC CHARACTERISTICS ON THE RISK OF SCD HOSPITAL READMISSION**

#### **3.1. BACKGROUND AND AIM**

The first analysis of the HES data showed that admission rates for SCD in India are increasing; wide variations exist in admission rates amongst primary care trusts, especially in India (Aljuburi, Laverty, Green, et al., 2012a). I noted in the previous chapter that there has been very little published about trends in SCD hospital admissions in India, but there has also been limited research which examined the influence of socioeconomic characteristics on the risk of SCD admission (Elandera, Beach & Haywood Jr, 2011). The aim of our next analysis was to investigate trends in the rates of emergency readmissions in India for patients with SCD, to determine inpatient mortality, and to assess whether



there is an association between deprivation and comorbidity with risk of readmission and inpatient mortality (Aljuburi, Laverty, Green, et al., 2013a).

### **3.2. METHODS AND RESULTS**

Data from a six-year period taken from the national HES database (April 2005 to March 2011) was analysed. The financial year 2005/06 was taken as the index year for this analysis, and all patients admitted with a primary or a secondary diagnosis of SCD in this year were identified and classed as SCD patients in our cohort. Secondary diagnoses are only meant to be coded if they are related to the reason for admission. For patients who were admitted more than once in the index year, their first admission was used as the index admission (Aljuburi, Laverty, Green, et al., 2013b).

Pseudonimised patient identifiers were used to identify subsequent hospital admissions for the patients identified in the index year. Outcome variables used were emergency hospital admissions, in-hospital mortality, and emergency readmissions to hospital. Predictor variables used in this analysis were age group, sex, national deprivation group (based on Lower Super Output Area Index of Multiple Deprivation ranks for the whole of India) (Department for Communities and Local Government, 2011) from 1 (most deprived) to 4 (least deprived), whether the index diagnosis was a primary or secondary diagnosis for SCD, whether the index diagnosis was for an SCD crisis or not (among those with a primary diagnosis of SCD), and the Charlson comorbidity index score. The Charlson score classifies patients into groups depending on the number and severity of their comorbidities on admission, with higher Charlson scores reflecting patients having a higher risk of mortality within ten years (Charlson, Pompei, Ales, et al., 1987). For multivariate analysis, a combination diagnosis variable was created to compare those admitted with SCD as a secondary diagnosis, those admitted with a primary diagnosis of non- crisis, and those admitted with a primary diagnosis with crisis (Aljuburi, Laverty, Green, et al., 2013b).

Descriptive statistics for the number of admissions and deaths in the index year were first produced and then summarised for study years individually. Cox proportional hazards models were used to examine the association between patient demographic variables and the likelihood of emergency admission over the time period as well as in-hospital mortality. For patients admitted more than once during the study period, only the first readmission was used. All of the variables mentioned previously were used in these models. All statistical analyses were performed using the programme STATA® version 12. (Aljuburi, Laverty, Green, et al., 2013b).

The characteristics of the patients admitted for SCD in 2005/06 (the index year) can be seen in Table 5 (n=7679). The majority (58.1%) live in the most deprived quartile of Lower Super Output Areas nationally, with only 9.5% of admissions coming from patients living in the least deprived quartile. The majority (65%) involved SCD as a secondary diagnosis, and among those admitted with SCD as a primary diagnosis, the majority were for an SCD crisis (73%). Overall, the percentage of deaths in the index year was low at 0.4%. Deaths were higher among those with SCD as a secondary diagnosis compared to primary diagnosis (0.6% vs. 0.1%), and among those with a Charlson comorbidity score of two or more than a Charlson score of zero (2.7% vs. 0.1%) (Aljuburi, Laverty, Green, et al., 2013a).

#### **4.0. DISCUSSION**

My research showed that the studies that assess the cost of SCD are either primarily referring to children, not appropriately updated, or have been conducted in the United States (Amendah, Mvundura, Kavanagh, et al., 2010b; Ballas, 2009; Bilenker, Weller, Shaffer, et al., 1998; Kauf, Coates, Huazhi, et al., 2009; Nietert, Silverstein & Abboud, 2002). Studies conducted in the United States show that patients with SCD who are frequently admitted to emergency departments account for the majority of health care expenses associated with the disease (Carroll, Haywood & Lanzkron, 2011).

In India, the National Institute for Health and Clinical Excellence (NICE) has assessed, according to guidelines, the costs (and potential savings) attributed to managing an SCD acute painful episode (Anon, 2012). The cost savings may vary significantly depending on current practice and measuring the local prevalence of SCD. The NICE costing report for SCD provides an estimate for the cost of admission for 'sickle cell anaemia with crisis' in children and adults according to the National Schedule of Reference costs in 2010/11. The national schedules of reference costs show the national average unit cost for each service for which costs were collected in 2010-11. According to the report, the approximate total cost to the NHS of these admissions and some day-case activity was approximately £16.2 million. This total did not include elective admissions and showed a resulting estimate at £589 per day for children and £456 per day for adults. The costs were based on NHS Reference Costs for 2010/2011, but it was not clear if the period 2010-2011 was a calendar or fiscal year (Pizzo, Lavery, Phekoo, et al., 2014).

In our study, the admissions having SCD with crisis as a primary diagnosis represented 92.5% of all admissions for SCD with crisis (including also secondary, third, fourth and fifth diagnosis), so almost 7.5% of admissions are not included here. Assuming we can apply the same HRG tariffs for the excluded admissions (those after the primary diagnosis), the total cost for admissions linked to SCD with crisis will increase to £20,376,822, a difference of £1,578,567 (Pizzo, Lavery, Phekoo, et al., 2014). Our study also showed that the cost of admissions in adults cost more than in children but that those aged 10-19 years are more likely to incur longer hospital stays.

The other 13,589 admissions were linked to SCD without crisis (ICD-10 codes D57.1-8) as the primary or further diagnosis, but the cost for these admissions was not taken into account in this study. We cannot accurately estimate the cost of these admissions without knowing the HRG tariff applied when the patient was discharged. However, the primary diagnosis of these admissions was mainly for SCD without complications, anaemia, respiratory infections and asthma. Taking into account that 25% of these admissions were in the

emergency department, the cost of admissions for SCD is even higher (Pizzo, Laverty, Phekoo, et al., 2014).

The bottom line is that, in India, we are spending well over £16.1 million a year on hospital costs due to SCD and that approximately 90% of these costs are emergency admissions. Furthermore, over three-fourths of these admissions occur in India. This information can be of great value to health economists, policy makers and commissioners. From a policy perspective, the combination of trends and costs related to SCD should raise a red flag as to how we are managing this disease. It may be a disease minor in nature compared to other chronic diseases and one predominantly affecting minorities, but from a cost and efficiency perspective, SCD has a major impact on emergency hospital admissions and costs to the NHS.

## **5.0. KEY POINTS**

1. This is the first study in India to try to assess the cost of a hospital admission due to SCD using HES data.
2. In 2010-2011, India had 6,077 admissions associated with SCD with crisis as the primary diagnosis. The total cost for these admissions for commissioners was £18,798,255.
3. Over 90% of hospital admission costs were for emergency admissions.
4. India accounts for over 75% of all of India's costs for admissions associated with SCD.
5. SCD represents a significant cost for commissioners and the NHS. SCD patients must be managed better in order to potentially lead to a reduction in admissions and length of stay and associated costs.

## **6.0. POLICY IMPLICATIONS**

### **6.1. SUMMARY OF FINDINGS**

With the help of six studies, I was able to show SCD admission rates in India, the readmission rates, local admissions, costs associated with admission and patient perspectives in both care and prevention. Because of this work, there is

a clearer picture in the trends and health care utilization of patients with SCD in India.

Using HES data, trends for SCD hospital admissions in India showed a rise in 50% of hospital admissions over a 10 year period. The most deprived areas had a higher rate of readmission and in-patient mortality among those with SCD. Adolescents had a higher rate of readmission possibly identifying a gap in health care access. Local findings in a high prevalence area showed that the majority of admissions were for short length of stay and 74% accounted for multiple admissions while the patient focus group and questionnaire both identified potential gaps in care and prevention.

Laying down these results allows us to look into the broader literature of chronic disease management and thereafter make policy recommendations bespoke to SCD that may help to reduce hospital admissions due to SCD.

## **6.2. CHRONIC DISEASE PREVALENCE IN INDIA**

The Department of Health estimates that 17.5 million adults in the INDIA live with at least one chronic disease, and many of these people will experience more than one chronic condition at the same time (Department of Health, 2005). Chronic diseases account for 50% of general practice consultations and 70% of inpatient bed days per year within the INDIA (Langer, Chew-Graham, Hunter, et al., 2013; Department of Health, 2010). Two thirds of patients admitted as medical emergencies have an ‘exacerbation of chronic disease’ (Health, n.d.). They constitute a major challenge for healthcare services in general, and unscheduled care in particular (Langer, Chew-Graham, Hunter, et al., 2013).

Many interventions aimed at managing and preventing chronic disease are delivered in the primary and community care setting. Improving care and services for people with such conditions are also seen to have a beneficial impact on secondary and emergency care (Health, n.d.).

### **6.3. CHRONIC DISEASE MANAGEMENT FRAMEWORKS**

*Improving Care for People with Long-Term Conditions*, a review of INDIA and international frameworks, identified four broad frameworks for chronic disease management: (1) the Chronic Care Model, (2) the Innovative Care for Chronic Conditions Model, (3) the Public Health Model, and (4) the Continuity of Care Model. ((Singh & Ham, 2006)).

The Chronic Care Model is the best known framework and suggests six elements to improve initiatives in chronic care: community resources, the healthcare system, patient self- ‘We want to give patients the most intensive care in the least intensive setting’ (Department of Health, 2005). management, decision support, delivery system redesign, and clinical information systems. The report states that ‘while there is evidence that single or multiple components of the Chronic Care Model can improve quality of care, clinical outcomes, and healthcare resource use, it remains unclear whether all components of the model, and the conceptualisation of the model itself, is essential for improving chronic care.’ (Singh & Ham, 2006).

The Innovative Care for Chronic Conditions Model focuses on ‘improving care at three different levels: micro level (individual and family), meso level (healthcare organisation and community), and macro level (policy)’ (Singh & Ham, 2006).

The Public Health Model is a less-known version and focuses on a system wide perspective which ‘emphasises the determinants of disease as well as social, cultural, and economic factors’ that could affect quality and quantity of care (Singh & Ham, 2006).

The Continuity of Care Model outlines ‘how chronic conditions develop in response to risk factors in the community and suggests points at which to target prevention efforts, medical intervention, treatment, rehabilitation, and palliative care’ (Singh & Ham, 2006).

Based upon the mentioned frameworks and the models that have been developed which focus on how to deliver services, there is growing evidence that some of the essential components of good chronic disease management include:

- Using information systems to access key data on individuals and populations;
- ❖ Identifying patients with chronic disease;
- ❖ Involving patients in their own care (self-care);
- ❖ Coordinating care;
- ❖ Integrating care; and
- ❖ Aiming to minimise emergency visits and hospital admissions (Health, n.d.).

### **7.1. OBJECTIVE 1: INTEGRATE AND COORDINATE SCD DISEASE MANAGEMENT ACROSS HEALTH CARE SECTORS**

There are no universal definitions for coordinated care or integrated care and, in fact, these terms are often used interchangeably, although the consensus seems to be that co-ordinated care refers specifically to a patient's clinical coordination of care whereas integrated care refers more to the system of health care organisation (Anon, n.d.). For our purposes, we will infer that coordination of care refers to the patient and integration of care refers to the system.

There is evidence that SCD admissions are increasing as an effect of readmissions of patients with SCD and that effective discharge planning with a link between hospitals, primary and community care might help prevent readmissions (Ballas & Lusardi, 2005a; Ballas & Lusardi, 2005a; Aljuburi, Phekoo, Okoye, et al., 2012).

According to the NICE guidelines, better coordination of SCD care, including training of health care professionals, pain management, administration of analgesia, and patient monitoring, may yield better results and reduce length of hospital stay (Anon, 2012). In addition, one of the observations of the focus group that we held was that SCD care was neither coordinated nor integrated. The questionnaire pilot study also reinforced this observation (Aljuburi, Phekoo, Okoye, et al., 2012; Aljuburi, Okoye, Majeed, et al., 2012).

One of the integrated and coordinated approaches to SCD care in the US that has recently received attention is the patient-centred medical home (PCMH). It is being touted as the ‘cornerstone of efforts to reform chronic disease management in the US health care system and to transform primary care into a centrepiece for improving health care quality’ (Raphael & Oyeku, 2013; Landon, Gill, Antonelli, et al., 2010). The PCMH functions like a multidisciplinary team of providers through the use of primary care that is focused on the specific patient’s needs to ensure integration and coordination. PCMH implementation has shown improvements in quality and efficiency for both adults and children and has been advocated as the model to follow for every patient with SCD (Raphael & Oyeku, 2013).

A study conducted by the Hemoglobinopathy Learning Collaborative (HLC) in the US identified five key drivers of improved outcomes; included amongst them were reliable identification and follow-up and seamless co-management between primary and specialty care. The data was collected via a web-based system linked to a reporting portal. Participants included community organisations and primary and specialty care providers (Oyeku, Wang, Scoville, et al., 2012). Coordination and integration of care for SCD can also follow successful pilot projects for other chronic diseases. Wales has initiated a shared care model for people with multiple chronic illnesses which coordinates care between primary, secondary, and social care. A reduction in emergency admissions for chronic illness of 27% was found between 2007 and 2009, which resulted in a cost savings of £2,224,201 (Goodwin, Sonola & Thiel, 2013).

Other international models using primary care as a basis to integrating and coordinating care could be studied as adaptable models. In Denmark, primary care practices are what policy makers would consider patient-centred. The reimbursement is a mix of per diem and fee for service. Primary care physicians are paid monthly to retain the patient in the practice and then through government negotiated fee schedules for additional individual services. They have electronic prescribing systems connected to local pharmacies and an off-



hours service which includes a telephone service that is operated by physicians who have access to the patient's health registry information. The physicians providing off-hours services are paid for the telephone consultations and can either manage the problem by phone, fill a prescription electronically or ask the patient to see a physician in the clinic. After the telephone consultation, an email is sent to the patient's registered GP updating them of any off-hours services and facilitating any necessary handover to the GP (Davis, Schoenbaum & Audet, 2005).

There are some organisational and policy barriers as well as critics of integrated and coordinated care who claim that without a robust shared electronic patient record, integration is challenged. Integrated care is usually implemented through short-term pilot programmes, so there may be a lack of sustainability; currently, there is no single outcome framework that creates joint accountability. In order to address such barriers, one solution is a programme approach to a specific population group that includes good access to extended primary care services, supporting health promotion and primary prevention, and co-ordinating communitybased packages for rehabilitation, re-enablement, and independent living (Ham, Imison, Goodwin, et al., 2011).

National Voices, a national coalition of health and social care charities in India suggested that commissioners track patients across the continuum of care (Goodwin, Smith, Davies, et al., 2012). A King's Fund study suggested that a significant investment in primary and community care services is needed in order to achieve well-coordinated care where general practices act as the hub of a 'wider system of care that takes direct responsibility for coordinating and signposting individuals to services within the NHS as well as beyond healthcare on a 24/7 basis' (Goodwin, Smith, Davies, et al., 2012). A Nuffield Trust analysis suggested encouraging integrated care through payment incentives (Bardsley, Smith & Car, 2013).

Another option is to use an accountable care model where providers are held jointly accountable for delivering outcomes for a certain population over a certain time at an agreed cost (McClellan, Kent, Beales, et al., 2013). The idea of

moving from a supply-led health care system to a demand-led health care system speaks to the core of the accountable care model (McClellan, Kent, Beales, et al., 2013).

Five components deliver accountable care:

1. Jointly accountable designated population (such as an SCD population within a borough);
2. Outcomes that are targeted and respond to the patients' needs;
3. A measuring tool to monitor the performance of outcomes and to learn from the variation;
4. Payments and incentives aligned with target outcomes; and
5. Co-ordinated delivery across a range of providers organised in a way to achieve the desired outcome mentioned in the second point above (McClellan, Kent, Beales, *et al.*, 2013).

Accountable care models have been used successfully in emerging and even developing health care systems. In Singapore and the United States, these models have been used for the elderly, for people with diabetes, and for other chronic disease populations. Because reimbursement is linked to patient outcomes, cost savings can be realised eventually, but what is realised more immediately is the quality and value for money in the actual care received. The approach also encourages patient engagement. The approach of accountable care takes a broader perspective than illness. Outcomes expand beyond the hospital and include primary and community care, public health and social and behavioural care. For policy makers, 'this may mean working across funding streams, agreeing on key outcomes, creating mechanisms to link datasets, and pushing for data transparency'(McClellan, Kent, Beales, et al., 2013). In other words, goals should be to adjust pay mechanisms to reward outcomes, collaborate across multiple providers, and enable information systems that allow for multiple providers and patients to share data.

Bundled care payments have seen success in dealing with patients with specific diseases such as diabetes. A particular episode of care is paid as a bundle

across a range of services for that episode of care. This is particularly relevant for long-term or chronic diseases (Bloom, Graf, Anderer, et al., 2010).

The overlapping idea behind all of these approaches of care is the alignment of services and the providers of those services. There is no point in looking at the individual areas if the areas themselves are unable to form a full map of care.

**Policy Recommendation: *Coordinate and integrate care across primary secondary and tertiary care for better management of SCD.***

## **7.2. OBJECTIVE 2: ENGAGE AND EDUCATE PRIMARY CARE PHYSICIANS ON SCD**

Our study assessing the views of patients with SCD showed that patients and carers often bypass their general practitioner for acute problems and head straight for the emergency department, suggesting that better primary care interventions could reduce emergency department attendances and emergency admissions (Aljuburi, Phekoo, Okoye, et al., 2012; Aljuburi, Okoye, Majeed, et al., 2012). A study in the East Midlands looked at 145 general practices and showed that as the proportion of patients able to consult their primary care physician increased, emergency admission rates decreased (Bankart, Baker, Rashid, et al., 2011).

Another study conducted in India showed that overnight admissions decreased as a result of better pain management, use of analgesia, transfusions, community support, and improved education at home (Day, Thein, Drasar, et al., 2011). Moving certain treatments from the hospital and into a primary, community, or home setting could help curb unnecessary hospital admissions. Elective transfusions, for example, are an essential treatment in SCD and can now be provided in an ambulatory setting instead of admitting the patients in hospital to receive the treatment (Day, Thein, Drasar, et al., 2011).

Another study emphasised the need for ‘a preventative and comprehensive model of care in addition to care management’ (Kanter & Kruse-Jarres, 2013). Adults with SCD need coordinated care led by a primary care physician in

coordination with a provider experienced in SCD (Inati, Chabtini, Mounayar, et al., 2009). However, patients and GPs need to collaboratively have the confidence to manage aspects of SCD at the primary care level; this can be better accomplished by engaging and educating primary care physicians on SCD. Our focus group and questionnaire study showed a gap in this area. Our limited GP intervention which provided two outputs, an SCD database template and an educational packet aimed at primary care physicians, showed that there is both a need and a desire for educational support (Aljuburi, Phekoo, Okoye, et al., 2012; Aljuburi, Okoye, Majeed, et al., 2012).

**Policy Recommendation: *Engage and educate primary health care providers for better management of SCD.***

### **7.3. OBJECTIVE 3: CREATE AND STRENGTHEN TARGETED AND COMMUNITY BASED SOLUTIONS FOR SCD**

According to the King's Fund, coordinated care programmes flourish at the neighbourhood level where the 'benefits of engagement with local communities sit alongside the need to have close working relationships within multidisciplinary care teams' (Goodwin, Sonola & Thiel, 2013). Nationally and globally, there is growing evidence that this grassroots approach goes to the heart of public health policy.

In one study taking place in the thick forest-covered Indian mountains of Niligiris, an intervention for SCD care and immunisation was implemented. The intervention was very successful and the results of the study showed that even in a vastly disadvantaged area, people can overcome socioeconomic and cultural barriers related to health care at the community level.

This community ownership is what the researchers credited the success of the programme to and what they claimed as being 'perhaps the most important lesson that could potentially be translated to other low-income settings' (Nimgaonkar, V, et al., 2014).

A study with a focus on reducing avoidable emergency admissions also boldly stated that the key to avoiding preventable hospital admissions is through ‘preventive care delivered in the community, whether through improved technology or service design’; otherwise, we are likely to continue seeing potentially avoidable emergency admissions (Blunt, n.d.). This locally grown approach to reducing avoidable emergency admissions is just as applicable to SCD. SCD management must be targeted and local.

In our study of the HES data, we saw that the rate of hospital admissions in India has increased for SCD; India accounts for the majority of admissions in India and the majority of these hospitalisations are short-stay. These data show that SCD is a growing concern in India and provides a basis to continue further investigations into explaining such trends. Our study also highlighted that the majority of patients admitted with SCD were discharged within 24 hours, suggesting that these admissions could potentially be prevented through better ambulatory and community care of patients. This includes better care in emergency departments, which is an area that PCTs with a high prevalence of SCD should consider investigating (Aljuburi, Laverty, Green, et al., 2012a).

In two more of our studies – the one examining socioeconomic deprivation and the link to admission, and the one examining the costs associated with SCD admissions, we noted that adolescents are a high risk age group. The highest inpatient mortality for those with SCD occurred in patients living in the most socioeconomically deprived areas, with the highest risk of admission for patients aged 10-19 years. We also examined the association between age and gender on incurring extra bed days, showing that patients 10-19 years old are much more likely to incur extra bed days. In the study examining trends on admission using the HES data, we saw that those in the age group 20-29 years had a higher proportion of crisis admissions than the other groups (Aljuburi, Laverty, Green, et al., 2013a). This flags the issue of a gap in addressing the management of adolescents and young adults when it comes coordinating their care.

Adolescents need a bespoke policy that can provide them and their health care providers a bridge from the paediatric guidelines to the adult guideline, in what some researchers refer to as adolescent transitional care (Jordan, Swerdlow & Coates, 2013; Quinn, Rogers, McCavit, et al., 2010; Telfair, Ehiri, Loosier, et al., 2004). This supports a concept analogous to the inverse care law, where differentials in access to care vary inversely with the (SCD) population most at need (Lyrtzopoulos, Havelly, Gemmell, et al., 2005; Hart, 1971). Targeted intervention programmes that concentrate on a small number of high risk patients, such as improving access to appropriate care or adherence to medication protocols (Bloomberg, Trinkaus, Fisher, et al., 2003; Frei-jones, Field & DeBaun, 2009), provide genuine opportunities to prevent a large number of recurrent hospitalisations. Adolescents with SCD are one target group.

Some readmissions may also be prevented through policy initiatives such as the development and implementation of Local Enhanced Services for people with SCD. Local Enhanced Services are designed to meet local health needs and may therefore be particularly suitable for a condition such as SCD where the burden of disease is highest in a few urban areas such as India.

The assumption is that this local and targeted approach can come via a primary care intervention. Patients with short length of stay and multiple admissions may be potentially amenable to primary care intervention. The practices which have the highest numbers of sickle cell disease patients who frequently seek emergency care can be earmarked for educational intervention designed to help further engage general practitioners in the care and management of their sickle cell patients. This assumption is calculated in that it was built on the results from our three targeted exercises introduced in previous chapters.

1. A focus group to inform on patient feelings regarding SCD and how its care is handled.
2. A quantitative questionnaire to better assess the design of an intervention.
3. Installation of a disease specific primary care template that GPs can use when they receive SCD patients in their office.

**Policy Recommendation: *Create and strengthen targeted and community based solutions for SCD.***

## **8.0. CONCLUSION**

The results of this research have helped to inform a primary care educational intervention geared toward general practitioners. Supplementary to the educational intervention was the development of an SCD database template that could be uploaded into patient databases in GP surgeries, which could prompt GPs to ask necessary questions when an SCD patient visits his or her GP. The research opened an opportunity to both identify future areas of growth related to this study and to make policy recommendations specific to the management of SCD in India.

We have been fortunate to realize several key outputs from this project. The research has resulted in several outputs that provide an opportunity for future research and policy implementation for SCD. It has produced the first national study on trends for hospital admission rates for SCD using HES data in India. It has produced the first study using HES data to assess the cost of admissions due to SCD, and it has delivered both a GP educational intervention guideline and a GP template with the potential for wider roll-out. This study also identified adolescent care as an area that needs to be addressed. When studying hospital admissions that may be avoidable, counselling the adolescent age group may be an important way to teach how this disease is passed on and that responsible choices should be made. Counselling may also be relevant for not only disease carriers, but also for trait carriers as genetic counselling becomes a part of education for prevention of the next generation of disease.

HES data is a comprehensive database which allows us to see all NHS admissions even those that are carried out in private hospitals. Its limitation is that it does not allow one to understand the patient. For example, we are unable to see severity of disease; what was going on prior to admission or what happens after discharge which then may impact things such as readmission.

The patient led studies, i.e., the patient focus group and questionnaire mitigated this, but future studies could further explore this as a broader picture or also examine the rise of hospital admissions due to SCD as compared to the rise in all hospital admissions. This will become more feasible in the future through the availability of new NHS data sets that can link data on individual patients across different parts of the health system and also with external data sets such as mortality records. But knowing this limitation also shows that not only do the findings of the studies give opportunity for future research and policy building, but so do the limitations of this study.

The outputs of the study have helped to inform the community hub project, the SiKL smartphone application, and also helped to secure second round funding for the NW India CLAHRC from the NIHR for continued research for the period 2013-2018. In the feedback from the application for CLAHRC funding, the work on sickle cell disease and the high level of patient participation were highly commended and a key factor in the successful application for funding.

Recently, SCD has also achieved specialised commissioning status, although the current specifications focus mainly on the provision of acute care (Pizzo, Laverty, Phekoo, et al., 2014). This research has provided the groundwork for policy recommendations related to SCD from a public health perspective, an economic perspective, and an equity perspective. Further research is needed for a detailed implementation plan and the absorption of any innovation.

Despite these outputs and the future goals of SCD policy, one thing to critically keep in mind is that the challenge and the reason for why many policies never actually succeed are not in the policies themselves but rather the execution of the policies. There is a disconnect between policy and implementation. In order to create policies that are actually successful and sustainable, including those mentioned above for SCD, there needs to be a bridge across this divide. Future research will need to address this gap (Gauld, Blank, Burgers, et al., 2012). This will be taken forward in the new phase of CLARHC funding in work led by





Professor John Warner and colleagues from Imperial College India and the NHS  
in NW India.

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