Institution:	**King's College London**
Unit of Assessment:	**2. Public Health, Health Services and Primary Care**
Title of case study:	***Sickle Cell Disease: Introduction of Population Screening Linked to Improved Treatment Services***

1. Summary of the impact

King's College London research identified the feasibility of implementing newborn screening for sickle cell disease, which was advocated. King's research also demonstrated the feasibility of antenatal screening for sickle cell disease early in pregnancy. A new national NHS Programme for antenatal and newborn screening for haemoglobin disorders was rolled out, with the national Programme Centre based at King's, resulting in increasing numbers of women and newborn infants being tested for sickle cell disease and trait. The screening programme enables informed choices for carrier individuals, and contributed to earlier diagnosis and better care for those with disease. King's research identified important problems in the delivery of treatment services for patients with sickle cell disease. The research informed the decision to designate specialist NHS services in order to address deficiencies in care.

2. Underpinning research

Sickle Cell Disease and Thalassaemia

Haemoglobin disorders, including sickle cell disease and thalassaemia, are the most common genetic disorders worldwide, primarily affect black and minority ethnic populations and contributing to inequalities in health. King's research led by Dr Allison Streetly (Senior Lecturer in Public Health, 1994-7; Honorary Senior Research Fellow, 1997-2013), Professor Theresa Marteau (Professor of Health Psychology, King's 1993 to 2012) and Dr Elizabeth Dormandy (SHIFT Trial Manager, later Deputy Director, Sickle Cell and Thalassaemia Screening Programme, King's 1999 to 2013); explored the feasibility of introducing a newborn screening programme for the condition; demonstrated the effectiveness of screening for haemoglobin disorders early in pregnancy; and evaluated the delivery of care for patients with sickle cell disease.

King's research identifies the potential to screen newborns for Sickle Cell Disease

King's research investigated the coverage of newborn bloodspot screening, as a potential means of screening infants for sickle cell disease (Streetly et al., 1994). This research found that overall coverage of bloodspot screening was 96% but there were important inequalities in coverage with lower screening coverage in infants of African ethnicity than in white infants. The research pointed out that the newborn bloodspot test could be used to screen for sickle cell disease but poorer coverage of infants of African origins might result in cases of sickle cell disease going undetected. The report authors advocated using the newborn bloodspot in screening for sickle cell disease in subsequent publications. The research showed that arrangements for monitoring the existing screening programme were inadequate and the research report recommended that an improved system for managing and monitoring the blood spot programme should be established.

King's research shows Sickle Cell carriers may be identified very early in pregnancy

King's research evaluated the potential for screening for sickle cell disease early in pregnancy. Dormandy et al. (2008) reported a study of 1,441 eligible women attending 25 general practitioner clinics offering universal antenatal screening. The median time interval between pregnancy confirmation in primary care and a screening test for sickle cell or thalassaemia being performed was 6.9 weeks, with only 4.4% of women being screened before 10 weeks gestation (Dormandy et al., 2008). The King's SHIFT cluster randomised trial provided evidence of the effectiveness, and impact on informed choice, of offering antenatal screening at the earliest stage of pregnancy in primary care (Dormandy et al., 2010a; Dormandy et al., 2010b). The SHIFT trial showed that in a conventional midwife-led model of care only 2% of women are screened for haemoglobin disorders before 10 weeks' gestation, compared with over 25% of women receiving general practitioner-led care with either parallel or sequential partner testing. These results showed that offering antenatal screening for haemoglobin disorders as part of consultations for pregnancy confirmation in primary care substantially increases the proportion of women offered screening before 10 weeks' gestation. This is important in enabling carrier couples to choose their preferred option in early pregnancy with less time pressure. Options may include prenatal diagnosis, with amniocentesis or chorionic

villus sampling, leading to possible termination of pregnancy.

King's research identifies problems experienced in seeking care for Sickle Cell Disease
King's research (Maxwell et al., 1999) showed that patients with sickle cell disease experienced substantial difficulties in hospital care. These were characterised by health professionals' mistrust of patients with sickle cell disease; their stigmatisation of sickle cell disease patients as potential drug addicts; professionals' control of treatment plans, diminishing opportunities for self-care; neglect of patients' personal care needs and monitoring of vital signs; and failure to offer psychological support. The research found that individuals who usually manage their pain at home showed different attitudes and strategies towards hospital services from those who are frequently admitted to hospital. The study recommended that models of care should be developed that acknowledge the diversity of the population with sickle cell disorders and prioritise the involvement and empowerment of patients in their care (Maxwell et al., 1999).

3. References to the research

Dormandy E, Gulliford MC, Reid EP, Brown K, Marteau TM; SHIFT Research Team (2008). Delay between pregnancy confirmation and sickle cell and thalassaemia screening: a population-based cohort study. *Br J Gen Pract* **58**:154-9. doi: 10.3399/bjgp08X277267.

Dormandy E, Bryan S, Gulliford MC et al. (2010a) Antenatal screening for haemoglobinopathies in primary care: a cohort study and cluster randomised trial to inform a simulation model. The Screening for Haemoglobinopathies in First Trimester (SHIFT) trial. Health Technol Assess **14**:1-160. doi: 10.3310/hta14200.

Dormandy E, Gulliford M, Bryan S, Roberts TE, Calnan M, Atkin K, Karnon J, Logan J, Kavalier F, Harris HJ, Johnston TA, Anionwu EN, Tsianakas V, Jones P, Marteau TM. (2010b) Effectiveness of earlier antenatal screening for sickle cell disease and thalassaemia in primary care: cluster randomised trial. *BMJ* **341**:c5132. doi: 10.1136/bmj.c5132.

Maxwell K, Streetly A, Bevan D (1999). Experiences of hospital care and treatment seeking for pain from sickle cell disease: qualitative study. *BMJ.* **318**:1585-90.

Streetly A, Grant C, Bickler G, Eldridge P, Bird S, Griffiths W (1994). Variation in coverage by ethnic group of neonatal (Guthrie) screening programme in south London. *BMJ*. **309**:372-4.

Research Grants
Evaluation of neonatal screening programme in Camberwell and West Lambeth. A Streetly. South East Thames Regional Health Authority, Locally Organised Research Scheme. 1992-1993.

A qualitative comparative investigation of sickle cell patients' experiences of pain management. A Streetly. King's Fund, Marks and Spencer, South Thames Region, Roald Dahl Foundation. £45,000. 1996-1998.

Antenatal screening for hemoglobinopathy: a cluster randomised trial. SHIFT Trial. T Marteau and 16 others. NHS R&D Health Technology Assessment Programme. 2004-2007. £599,000.

4. Details of the impact

King's research has achieved impact in the field of sickle cell disease through its contribution to the roll-out of an antenatal and newborn screening programme, linked to designated NHS specialist treatment services for haemoglobin disorders. The principal beneficiaries are people with sickle cell disease and their families whose management has moved from the margins of the NHS to the mainstream. Individuals with sickle cell disease have benefited from earlier diagnosis and better treatment. Carriers of the sickle cell trait have benefited through being enabled to make informed reproductive choices when a pregnancy may be affected.

King's hosts the national Screening Programme Centre

Following up the research on newborn bloodspot coverage, King's was commissioned by the Department of Health to implement a National Audit of the Newborn Bloodspot Programme. As a result of a 1999 workshop convened by the National Screening Committee (NSC), at which the King's research on bloodspot programme coverage was presented alongside the results of two Health Technology Assessment reviews, universal newborn screening for sickle cell disease was recommended. In 2000, the Department of Health committed to introduce newborn and antenatal screening for haemoglobinopathies including sickle cell disease and thalassaemia. The National Programme Centre for the NHS screening programme was established at King's College London from 2000 to 2013 through a contract between the Department of Health and King's, which had a value of £7.75 million in the period 2008-2013. The Programme was directed by Dr Streetly (2000-2013), reporting to Dr Anne Mackie as Director of Programmes, for the National Screening Committee. The Programme Centre transferred to Public Health England in 2013. The aim of the NHS Haemoglobinopathy Screening Programme is to support people to make informed choices during pregnancy and before conception, to improve infant health through prompt identification of affected babies, to provide high quality and accessible care for these conditions throughout England and promote greater understanding and awareness of the disorders (NHS Sickle Cell and Thalassaemia Screening Programme, 2013).

King's leads implementation of the National Screening Programme

With national leadership based at King's, universal newborn and antenatal screening for sickle cell disease was introduced in England while implementation in Scotland and Northern Ireland was also supported. This was achieved through setting standards (Ryan et al. 2010); designing pathways for screening and care; education and training; establishing communications and preparing materials for professionals and the public; establishing data collection systems for surveillance and monitoring; and quality assurance and evaluation. The main impacts of the screening programme roll-out in England are summarised in the Table including results from the Screening Programme Data Reports from 2008/9 to 2011/12 (NHS Sickle Cell and Thalassaemia Screening Programme 2013).

Programme Impacts for England	**2008/09**	**2009/10**	**2010/11**	**2011/12**
Newborn infants screened	669,427	648,317	688,314	693,278
Significant clinical condition identified	360	361	358	320
Carriers identified	9,624	9,732	9,830	9,718
Antenatal women screened	657,160	643,671	723,768	733,610
Screen positive sickle or thalassaemia	22,305	16,135	17,354	16,556
Fathers offered test	18,500	16,670	15,908	15,681
Partners tested	10,279	9,554	9,028	9,465
'At risk' pregnancy	938	1,006	940	918
Prenatal diagnosis procedures	388	396	420	418
Affected foetus identified	88	102	95	101

Newborn screening has increased the number of children being identified with sickle cell disease, in many areas almost doubling the service workload (Streetly et al., 2009). The King's group proposed that under-ascertainment of the condition may have allowed a downplaying of the scale of need and contributed to infant mortality rates in urban areas as babies died without a diagnosis or treatment (Streetly et al., 2009).

Influenced by the results of King's SHIFT Trial (whose Trial Manager, Dormandy, became Screening Programme Deputy Director), the national NHS Screening Programme has set a minimum standard of requiring 50% of prenatal diagnosis procedures to be implemented by 12 weeks and 6 days gestation. The Data Report for 2011/12 (NHS Sickle Cell and Thalassaemia Screening Programme, 2013) (Table AN-4) shows that 61% of all initial antenatal screening tests in England are now performed by 12 weeks gestation. This has been accompanied by an increase in the number of pre-natal diagnosis procedures being performed from 307 in 2004/5 to 418 in 2011/12, with 52% of these now being performed within 12 weeks 6 days of gestation (Table PND-6).

King's provides international advice on haemoglobinopathy screening

During the assessment period, the Screening Programme has benefitted from strong stakeholder involvement, with the Archbishop of York chairing the Programme Steering Group. There has been international interest in the screening programme, which is recognised to be the best developed in Europe, and arguably the world, providing a model for many other countries. Dr Streetly has given invited presentations at the Centres for Disease Control, Atlanta, USA, Ghana, and in Europe in Rome, Lisbon, Barcelona, Paris and Berlin. The Programme has also hosted visits from, or provided advice to, public health advisers to the Netherlands government, US Centres for Disease Control, Sri Lanka and Nigeria among others. The Programme website is regularly accessed and materials downloaded by interested parties from across the world.

King's research stimulates action to improve patient care and specialist treatment services

King's research drew attention to the difficulties that patients with sickle cell disease experience in their interactions with hospital services. Following on from the research, a National Confidential Enquiry into Patient Outcomes and Death (NCEPOD, 2008) into sickle cell disease was launched. King's contributed to the authorship of the NCEPOD report (Professor Sebastian Lucas, Dr Allison Streetly). The NCEPOD findings confirmed and extended the results of the King's research. Of 35 sickle cell disease patients who died in hospital, 19 had pain as an admitting complaint. In nine patients excessive doses of opioids were judged to have been administered, contributing to the patient's death in five cases. The NCEPOD report made 28 specific recommendations for the improvement of clinical treatment and service delivery for sickle cell disease including better management of acute pain and improved care of the long-term illness by clinicians with specialist expertise and training. The recommendations were circulated to Medical Directors of all Trusts for action. Recognising the need for action to improve the quality of care highlighted by this report, the Department of Health commissioned a National Haemoglobinopathies project that produced guidance for commissioners on effectively commissioning high quality sickle cell and thalassaemia services. The guidance included designated standards that Trusts must deliver to secure specialist status for haemoglobinopathy care as well as model service specifications and a commissioning framework. The final NHS guideline document (NHS East Midlands 2011) included an endorsement written by Dr Streetly from King's in her capacity as Programme Director of the National NHS Haemoglobinopathy Screening Programme. The Department of Health also prioritised this as an area for National Institute for Health and Care Excellence (NICE) guidance leading to sickle cell crises being defined as an emergency condition (NICE, 2012).

5. Sources to corroborate the impact

National Institute for Health and Care Excellence (NICE) (2012) Sickle cell acute painful episode (CG143) Appendix E. London: NICE: page 101, Table 82.

NCEPOD (2008). A sickle crisis? A report of the National Confidential Enquiry into Patient Outcome and Death. London: NCEPOD:

NHS East Midlands Specialist Commissioning Group (2011). The National Haemoglobinopathies Project. A guide to effectively commissioning high quality sickle cell and thalassaemia services. (page 7)

NHS Sickle Cell and Thalassaemia Screening Programme (2013): Website

Data report 2011/12	Programme Review 2011/12
Data report 2010/11	Annual Report 2010/11
Data report 2009/10	Annual Report 2009/10
Data report 2008/09	Annual report 2008/09

Ryan K et al. (2010). British Committee for Standards in Haematology. Significant haemoglobinopathies: guidelines for screening and diagnosis. *Br J Haematol.* **149**:35-49. doi: 10.1111/j.1365-2141.2009.08054.x.

Streetly A, Latinovic R, Hall K, Henthorn J (2009). Implementation of universal newborn bloodspot screening for sickle cell disease and other clinically significant haemoglobinopathies in England: screening results for 2005-7. *J Clin Pathol* **62**:26-30. doi: 10.1136/jcp.2008.058859