Hospital Resource Usage and Costs for Patients With Sickle Cell Disease in England: a 10-year Cohort Analysis

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Research Article

Keywords: Sickle cell disease (SCD), Hospital Episodes Statistics (HES), Hospital resource, usage and costs, patients, England

Posted Date: October 20th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-920004/v1

Abstract

Sickle cell disease (SCD) is one of the most prevalent serious genetic conditions in England. Increased patient numbers and more intensive management is thought to have resulted in higher demand for hospital services. This study attempts to quantify this increase.

Data from the Hospital Episodes Statistics (HES) Admitted Patient Care (APC) and Outpatient (OP) datasets for patients with a diagnosis of SCD during the 10-year period January 2009 to December 2018 were extracted. Two sub-groups were defined, 'high crises' and 'high transfusions', with all other patients assigned to the 'other SCD' group. Analysis of hospital resource use in the three sub-groups was undertaken.

Overall patient numbers increased by 9.9% (9,615 to 10,570) and treatment costs by 82% (£41.9m to £76.4m) over the ten-year period. Disproportionately greater: patient numbers and costs were observed in the two sub-groups of interest. In the high crises sub-group, patient numbers increased by 43% (1,194 to 1,713) and treatments costs by 310% (£9.4m to £38.5m), with corresponding increases of 187% (205 to 589) and 236% (£2.8m to £9.4m) in the high transfusions patients sub-group.

Prevalence of sickle cell disease in England continues to grow resulting in significant demand on NHS services. Patients categorised as high crises and high transfusions are consistently greater users of hospital resource and account for the majority of NHS hospital expenditure.

Introduction

Sickle cell disease (SCD) is a serious, lifelong condition, and is one of the most prevalent genetic conditions in England.[1] It is a progressive, unpredictable, and debilitating disease caused by a single mutation in the β-globin gene that leads to production of sickle haemoglobin (HbS).[2] SCD affects both adults and children[1], causes a wide range of acute[3] and chronic complications, substantially reduces life expectancy[4,5,6,7,8], and often requires high hospital resource use.[9] Patients are commonly admitted to hospital for the management of acute pain, anaemia, acute chest syndrome, infection, and to receive regular blood transfusions.[8] Most SCD patients also require continued out-patient care usually involving multi-disciplinary teams.[10]

A previous analysis of the Hospital Episodes Statistics (HES) database in England explored SCD admissions over a nine year period from 2001-2010.[8] Since these data were published, the number of patients with SCD has been expected to grow with the roll-out of a national screening programme supporting the identification of SCD at birth.[11,12] Additionally, a higher priority has also been placed on the effective management of SCD as evidenced by the recent National Institute for Health and Care Excellence (NICE) quality standards, clinical guidelines, and specialised commissioning arrangements.[9,13,14,15,16] Both of these factors are likely to have resulted in higher demand for hospital services, although evidence of the extent of this increase has thus far been lacking.

To address this gap, we conducted a retrospective analysis of HES data quantifying hospital resource use and admitted patient and out-patient costs of managing patients with SCD in England over the 10-year period from 2009-2018.

Methods

Data Sources

The HES database is derived from data on hospital activity in National Health Service (NHS) hospitals in England. All NHS hospitals are required to submit activity data to NHS Digital, the national provider of data and IT systems for commissioners, analysts, and clinicians in health and social care. The HES database is pseudonymised by redaction of identifying details and each patient is allocated a unique identifier, allowing hospital activity to be tracked over time. The HES database contains several datasets, including HES Admitted Patient Care (APC) and HES Outpatient (OP). HES APC records all inpatient admissions by NHS patients in English hospitals. Each admission is comprised of one or more Finished Consultant Episodes (FCE), a period of admission under the care of a particular consultant which records patients' demographic details, a primary diagnosis (reason for admission), and up to 23 secondary diagnoses that are relevant to patients' care during their admission. Diagnoses are coded using the World Health Organisation's International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10).[17] Procedures and interventions are recorded using the OPCS-4.8 classification system.[18] Ethnicity is recorded using Office for National Statistics (ONS) categories.[19] The HES OP dataset records patient demographics and details of outpatient appointments (e.g., date, speciality, and consultant or non-consultant appointment). It is not compulsory for hospitals to record diagnoses in the OP dataset and these are usually omitted. HES records can be matched to the date and cause of death recorded by the ONS, capturing deaths both in and out of hospital.

Our analysis involved no live animal or human subjects. All methods were performed in accordance with the relevant guidelines and regulations. For this analysis, data were extracted from the HES APC dataset for all patients with one or more primary diagnoses of either SCD with crisis (ICD-10 Code D57.0) or SCD without crisis (ICD-10 Code D57.1) during the 10 years from January 2009 to December 2018. For these patients, data were also extracted from the HES OP dataset and the HES ONS mortality dataset. As HES does not record the genotype of SCD for each patient, it was not possible to examine genotypic variants.

Data were cleaned to remove duplicate patients with invalid years of birth (<1900) by matching them with valid patients (based on sex, general practice (GP), Trust attended, and consultant) and to exclude patients without a valid English GP practice, and patients where SCD was not the most commonly diagnosed haemoglobinopathy.

Resource Use and Costing

FCE level HES APC data were grouped to admissions and allocated a 2017/18 Healthcare Resource Group (HRG) using the NHS Grouper Software. HRGs are groups of healthcare services considered to have similar resource requirements. The Grouper Software allocates an HRG to each admission using an embodied ruleset based on the diagnoses and procedure coding in its component FCE's.[20] HES OP data were similarly grouped and allocated an HRG.

To avoid the impact of inflation or other fluctuations in costs over the study period, activity in all years was costed using the 2017/18 NHS Reference Costs at an FCE level.[21] Admissions for birth were excluded and dialysis episodes were not costed, as HES APC does not contain all the detail required. Where HES OP data lacked detail to distinguish between consultant led and non-consultant led appointments, these were costed at a speciality level using the average split between consultant led and non-consultant led appointments for which data were available.

Statistical Analysis

For hospital admissions, costs and admission numbers were allocated hierarchically to one of five categories: i) allogeneic haematopoietic stem cell transplant ("allo-HSCT"); ii) sickle cell crisis (those admissions containing an ICD-10 code of D57.0 whether as a primary or secondary diagnosis); iii) transfusion (those containing an OPCS code for an exchange or top-up blood transfusion); iv) other SCD (those admissions containing an ICD-10 code of D57.1 whether as a primary or secondary diagnosis) and v) other-non-SCD admissions (those admissions with no D57.0 or D57.1 diagnosis codes or allo-HSCT or transfusion OPCS codes). For outpatient appointments, costs and appointment numbers were allocated to one of two categories: i) haematology, or ii) other.

Patients were followed from January 2009 or birth, to death or December 2018. Trends in patient numbers, hospital resource usage, and costs during the ten years for each patient group and in total were examined in absolute terms as well as in compound annual growth rates (CAGR).

Sub-group Analysis

Following data cleaning, statistical analysis was undertaken on all SCD patients and on two sub-sets of patients; those with four or more admissions for sickle cell crisis over any two-year period (termed 'high crises' patients) and those with six or more blood transfusions in each year of any two-year period (termed 'high transfusions' patients). Where patients met both definitions, they were allocated to the high crises sub-group.

Results

Patient Characteristics and Numbers

A total of 16,680 patients with a primary diagnosis of SCD, with or without crisis, were identified, for which data were extracted. Data were de-duplicated for patients with no valid year of birth recorded (2,538 matched to valid patients, 730 unmatched and excluded). Further exclusions were: i) not registered to a GP in England (2,117); and ii) SCD not the most commonly recorded haemoglobinopathy (194). After data cleaning, 11,101 SCD patients were included in the analysis, of which 48% were male. The mean age at first hospital admission was 20.8 years (median: 18, inter-quartile range (IQR): 5-32). The mean length of follow-up was 9.4 years (median: 10.0, IQR 10.0-10.0). Reported ethnicity was 77% Black, 5% White, 4% Mixed, 4% Other, 2% Asian, and 9% not reported/not stated. The number of patients with SCD alive in January 2009 was 9,615. During the 10-year period, 1,486 patients were born and 531 died; leaving 10,570 patients alive at the end of 2018. The net increase of 955 patients over the study period represents a 1.0% combined annual growth rate (CAGR).

Hospital Resource Usage

APC data were extracted for 361,518 FCEs which grouped to 313,791 admissions. Outpatient data were extracted and grouped for 582,374 appointments. Mean annual hospital admissions per patient increased by 6.2% per annum over the analysis period, from an average of 2.15 per patient in 2009 to 3.70 in 2018 (Table 1). Increases in admissions for sickle cell crises accounted for 48.4% of the increase in admissions, with increases in transfusions accounting for 33.6%. Only non-SCD admissions (i.e. those with no reference to SCD, sickle cell crisis, transfusion, or allo-HSCT in their diagnoses and procedure coding) decreased over the study period. Mean outpatient attendances increased by 5.9% per patient per annum. Over the 10-year period, there were 115 allo-HSCT procedures in 109 patients.

Hospital Costs

Of the 313,791 admissions, 296,737 (94.5%) could be costed; the remaining balance related principally to renal dialysis, which cannot be accurately costed in the HES dataset. 581,593 of 582,374 outpatient appointments were costed (99.9%). Total hospital costs for all patients for the 10-year period were £604.1m, comprised of £513.2m for hospital admissions and £90.9m for outpatient appointments. Annual costs increased from £41.9m to £76.4m over the study period, reflecting a CAGR of 6.9%. Increasing costs for crises admissions (7.5% CAGR) and transfusions (10.7% CAGR) were the main drivers of the increased total costs (Figure 1).

Sub-group analysis

The number of high crises patients increased from 1,194 in 2009 to 1,713 in 2018 (4.1% CAGR). Total admitted care and out-patient costs associated with these patients grew from £19.4m in 2009 to £38.7m in 2018 (8.0% CAGR). Similarly, the number of high transfusions patients increased from 205 in 2009 to 589 in 2018 (12.4% CAGR), and the costs associated with these patients grew from £2.8m in 2009 to £9.4m in 2018 (14.3% CAGR) (Figure 2).

Both high crises and high transfusions patients, as defined in 2009 & 2010, went on to have total 10-year hospital costs over four times higher than other SCD patients (Figure 3). For the 1,194 high crises patients in 2009 & 2010, hospital costs in 2009 & 2010 were a mean £16.8K per patient per annum. In the subsequent eight years, 2011-2018, costs were £17.2K per patient per annum. A similar pattern was observed for the 205 high transfusions patients. Costs in

2009 & 2010 were a mean £14.2K per patient per annum, rising to £17.1K in 2011-2018. For both high crises patients and high transfusions patients (as defined in 2009 & 2010), costs were more than £11K per year higher than for other SCD patients in 2009 & 2010 and more than £12K per year higher in the remaining eight years, 2011-2018.

Discussion

Main findings of this study

This study indicates that growth in hospital activity and in costs for patients with SCD over the 10 years to 2018 has occurred at a considerably higher rate than growth in the total number of admitted SCD patients. Most of the growth has come from increasing per patient admission rates for sickle cell crises and transfusions.

When measured at constant 2017/18 Reference Costs, the cost of treating SCD patients grew from £41.9m in 2009 to £76.4m in 2018 (CAGR 6.9%). This is in line with the 0.8% per annum increase in SCD patient numbers and the 6.2% per annum increase in admissions per patient.

Our analysis indicates that the increase in SCD patients admitted to hospital over the 10 years to 2018 (9.9%, 1.0% CAGR) is consistent with the growth in the English population over the same period. Rising SCD admissions and costs are therefore principally due to rising admission rates per patient (6.2% per annum), rather than due to a disproportionate increase in numbers of patients (0.8%).

High crises patients and high transfusions patients represented a growing proportion of the SCD patient population in England. These patients are mostly high users of hospital resource and account for the majority of NHS hospital expenditure on SCD patients. In 2018, high crises and high transfusions patients represented 22% of the SCD admitted patient population, but accounted for 62% of hospital expenditures.

What is already known on this topic

A previous analysis of the HES database by Aljuburi *et al* reported a 58.0% increase per capita in SCD admissions (defined as admissions with a primary diagnosis of D57.0 or D57.1) in England over the period April 2001 to March 2010 (5.4% CAGR).[9] This is similar to the 72.0% (6.2% CAGR) increase in admissions per SCD patient during 2009-2018 found in this study. Although there are some differences in definitions and analytical approach between Aljuburi *et al* and this study, it is clear that admissions for SCD have been increasing substantially over the last 20 years.

The rate of patient growth that we observed may seem low compared with the results of the NHS Sickle Cell and Thalassaemia Screening Programme which identified 3,857 newborns with results indicative of SCD in the 12 years between April 2005 and March 2017, an average of 321 per year.[10] By contrast, post-2009, we observed an average of 143 children born with SCD per year admitted for the first time during the study. The Screening Programme identifies infants who, on further investigation, have clinically insignificant variants of SCD or who emigrate shortly after birth. Approximately 82% of positive screens result in an infant attending a specialist SCD out-patient clinic within 3 months of birth, rising to 98% within 6 months of birth.[22] A similar picture emerges with regard to prophylactic antibiotic use, with 83% prescribed penicillin by 3 months and 97% by 6 months of age.[21] It's possible that the Screening Programme, which was implemented in England between 2003 and 2006, i.e. several years before this study period, may have reduced admissions in children with SCD, accounting for some of the gap between the Screening Programme and children born post-2009 with first admissions seen in this study.

There are no definitive data on SCD prevalence in the United Kingdom. The West Midlands Quality Review Service in their 2014-2016 peer review programme reported 12,175 SCD patients registered at centres in England.[23] Dormandy *et al* reviewed all national SCD databases and estimated an SCD prevalence in England of 13,655 in 2017.[1] Therefore, there are approximately 2,000-3,000 SCD patients who did not form part of our study because they were not admitted in the 10-year study period. This cohort likely comprises patients with clinically mild forms of SCD who may never be admitted, whilst others will likely require hospital care in the future as their disease progresses.

What this study adds

This study adds a contemporary 10-year perspective on the burden of SCD on the NHS in England, focusing on the two highest cost areas, admitted patient care and out-patient appointments. By using the ability of HES data to follow patient hospital activity over time, we have been able to select and quantify two groups of SCD patients (high crises patients and high transfusions patients) whose prevalence, resource use, and associated hospital costs have been growing rapidly and disproportionately to the overall growth of the SCD population.

Whilst HES data can inform on variability in hospital utilisation, the underlying reasons for such variability are probably mostly attributable to changes in guidelines and management strategies. The increase in sickle cell crisis admissions may be explained by a lowering of the threshold for admission for sickle cell patients caused by greater awareness and recognition of the need for acute management, and monitoring of patients with possible disease-related complications. Increases in transfusion numbers likely reflect changing clinical practice in recent years to greater utilisation of regular blood transfusions for primary and secondary stroke prevention, particularly in children, supported by the increased availability of automated exchange transfusions which have been deemed a cost-effective intervention by the NICE[24]. Transcranial Doppler monitoring, iron monitoring associated with regular transfusions, and regular blood counts required with use of hydroxycarbamide may all contribute to the increase in other SCD admissions (where such procedures are performed on a day case basis) and out-patient appointments.

SCD is now the most common serious inherited genetic disorder in England, however there is a distinct lack of literature on the resource utilisation implications of the condition on healthcare systems in the United Kingdom, or indeed other developed countries. Given the present burden as well as the

evolving therapeutic landscape for this complex disease[25], it is relevant and important to evaluate resource utilisation and cost-consequence of the present clinical paradigm on health systems and budget holders.

Limitations of this study

NHS Digital requires hospitals to audit the accuracy of their clinical coding annually and achieve 90% or more accuracy in primary diagnosis coding, and 80% or more in secondary diagnosis coding.[26] Nevertheless, the quality of clinical coding in the NHS varies over time, and between trusts and disease areas. Though no specific study of coding accuracy in SCD exists, a systematic review of 32 clinical coding accuracy studies during the period 1989 to 2011 found that the median accuracy of NHS primary diagnosis coding was 80.3%, but that this had increased to 96.0% after the introduction of Payment by Results in 2002.[27]

We acknowledged above the existence of SCD individuals not included in this study. These missing individuals did not affect our results for hospital admission numbers and costs as they were not admitted to hospital during the study period. However, as most of these individuals were probably monitored in an outpatient setting, outpatient activity and costs may be understated.

This study has not examined the impact of cohort aging on resource usage, or of geographical variations within England. The median age of patients alive at the start of 2009 was 21.0 years. At the end of 2018, this had increased to 26.6 years. An aging cohort is likely to require more hospital care as complications of SCD manifest. Although the vast majority of SCD patients are in London, it is likely that resource usage and costs vary between hospitals.

Finally, not all costs were captured in this analysis (e.g. costs of dialysis or costs of treatment outside a hospital setting). The activity and costs of patients with a GP practice outside England who accessed hospitals in England are also excluded.

Declarations

Acknowledgements

The HES database is Copyright © 2019, and is re-used with the permission of NHS Digital. All rights reserved. Editorial assistance was provided by insight 2 implement Ltd. Beacon Consulting provided editorial assistance and specific expertise on the HES database. Funding was provided by bluebird bio (UK) Ltd and bluebird bio Inc.

Contributions

M.J., M.G. and J.W. designed the study; M.M. and M.J. developed the coding framework; M.M analysed the data: S.L. and M.M. wrote the paper. F.P. provided disease-area expertise. All authors reviewed the manuscript and agreed the final content prior to publication.

Ethics Declarations

F.P. received an honorarium from bluebird bio Inc; M.J. is an employee of bluebird bio (UK) Ltd, with stock ownership in bluebird bio Inc; M.G and J.W. are employees of bluebird bio Inc with stock ownership; S.L. is an employee and Director of insight 2 implement Ltd. which has been retained by bluebird bio Inc for manuscript development; M.M. is a Director of Beacon Consulting and which has been retained by bluebird bio Inc. to develop the coding framework, analyse the data and develop the manuscript. The study was funded by bluebird bio, Inc. bluebird bio Inc. has an investigational gene therapy in development for a subset of patients with sickle cell disease.

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Table

Table 1
Patient numbers and hospital resource usage of all SCD patients by year, 2009-2018.

Year	Patient numbers (alive during year)				Unique patients admitted during year	Mean APC admissions per patient*						Mean OP records per patients*		
	Alive (at start of year)	Born†	Died	Alive (at end of year)		Allo-HSCT	Sickle cell crisis	Transfusion	Other SCD	Other non-SCD	Totals	Haematology	Non-haematology	T
2009	9,615	284	36	9,863	4,870	0.0004	0.74	0.43	0.59	0.39	2.15	1.86	2.33	4
2010	9,863	210	46	10,027	5,175	0.0005	0.84	0.47	0.59	0.43	2.33	2.01	2.52	4
2011	10,027	234	42	10,219	5,301	0.0007	0.92	0.55	0.58	0.42	2.48	2.26	2.66	4
2012	10,219	201	37	10,383	5,650	0.0006	1.02	0.63	0.74	0.38	2.77	2.33	2.80	5
2013	10,383	171	55	10,499	5,681	0.0010	1.19	0.66	0.72	0.36	2.93	2.45	3.01	5
2014	10,499	135	48	10,586	5,743	0.0017	1.33	0.72	0.74	0.40	3.18	2.54	3.08	5
2015	10,586	108	58	10,636	5,916	0.0015	1.34	0.82	0.82	0.38	3.37	2.67	3.18	5
2016	10,636	85	70	10,651	6,035	0.0016	1.34	0.92	0.89	0.40	3.55	2.81	3.49	6
2017	10,651	50	66	10,635	6,026	0.0018	1.40	0.90	0.88	0.37	3.56	3.07	3.69	6
2018	10,635	8	73	10,570	6,219	0.0012	1.49	0.95	0.92	0.34	3.70	3.24	3.76	7
Totals		**1,486**	**531**			**0.0109**	**11.60**	**7.06**	**7.48**	**3.87**	**30.03**	**25.24**	**30.52**	5
Total growth 2018 vs 2009 (%)				**9.9**	**27.7**	**203.3**	**101.8**	**121.0**	**56.1**	**13.6**	**72.0**	**66.9**	**74.2**	6
CAGR (%)				**1.0**	**2.8**	**13.1**	**8.1**	**9.2**	**5.1**	**-1.6**	**6.2**	**5.9**	**6.4**	5

** Denominator is number of patients alive at end of year.* † Refers to year of birth, not year of first admission.

CAGR: Compound Annual Growth Rate; APC: Admitted Patient Care; OP: Outpatient

Figures

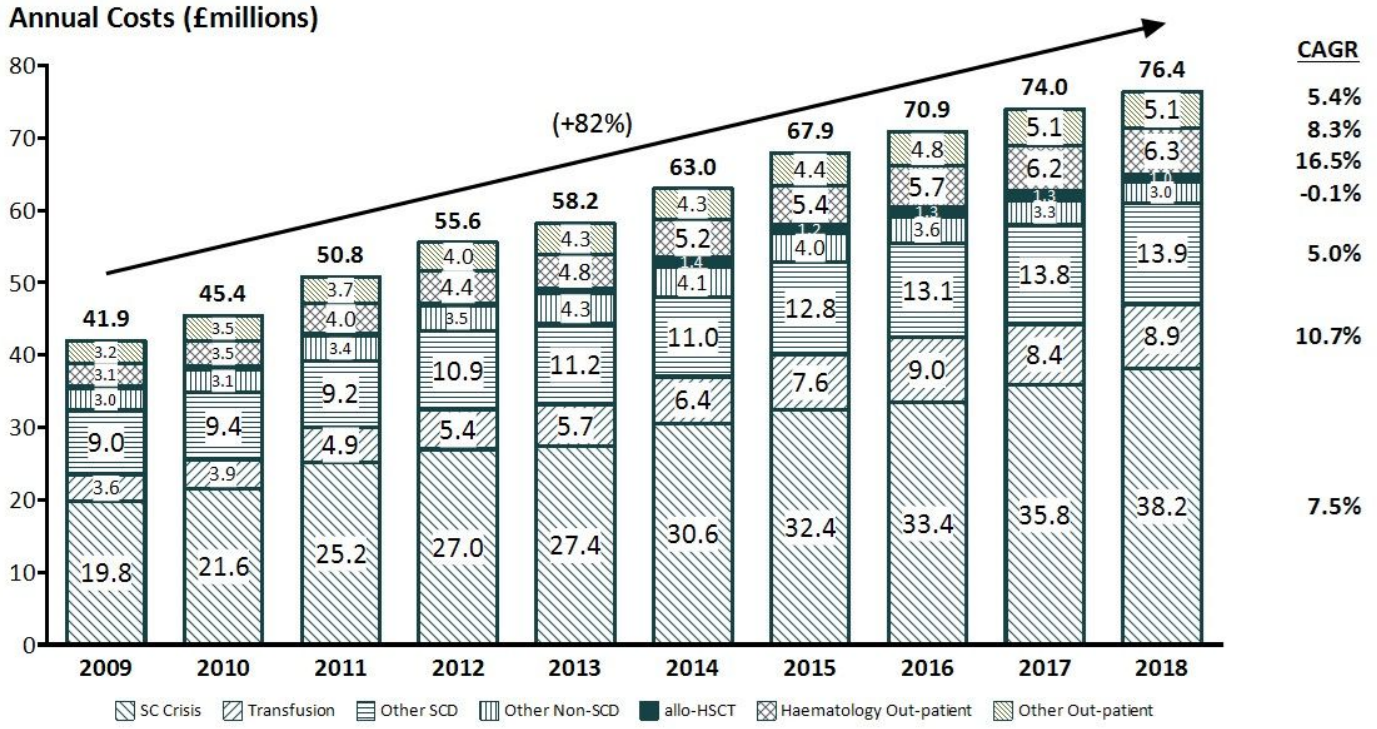
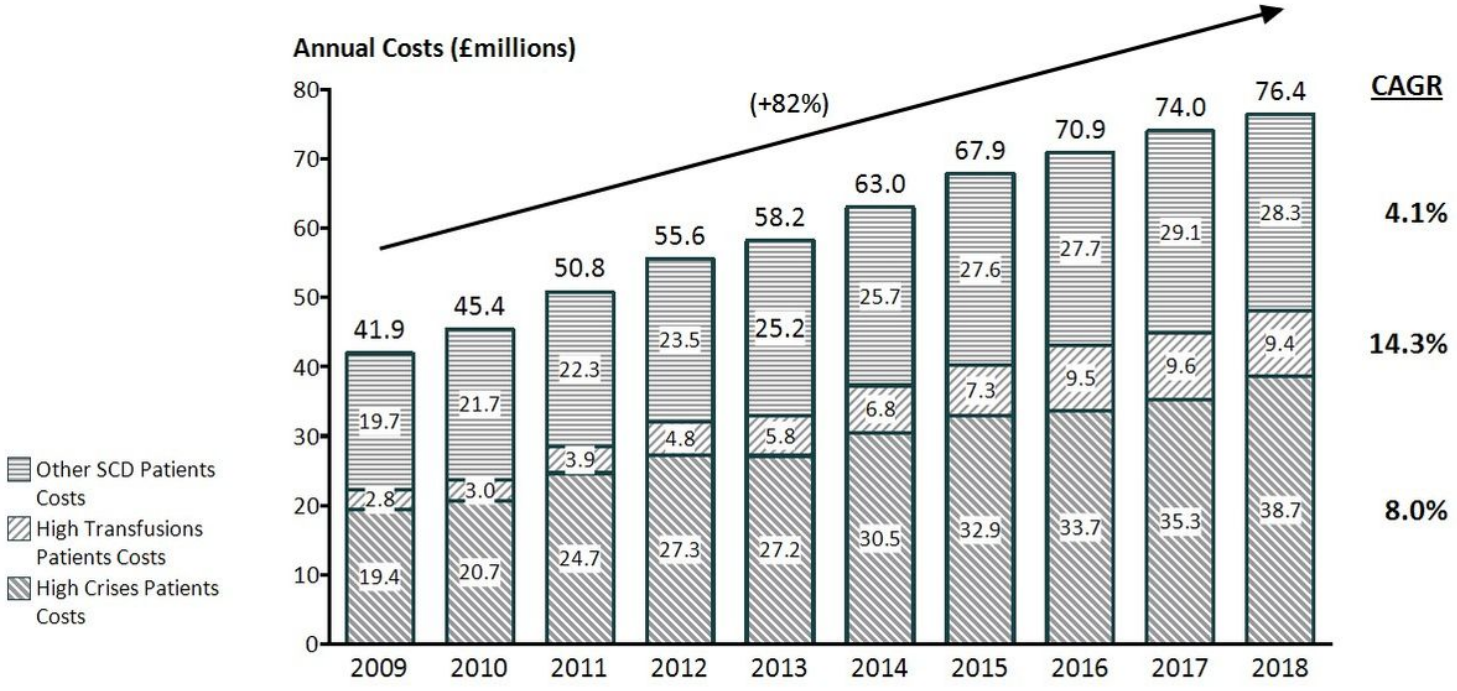


Figure 1

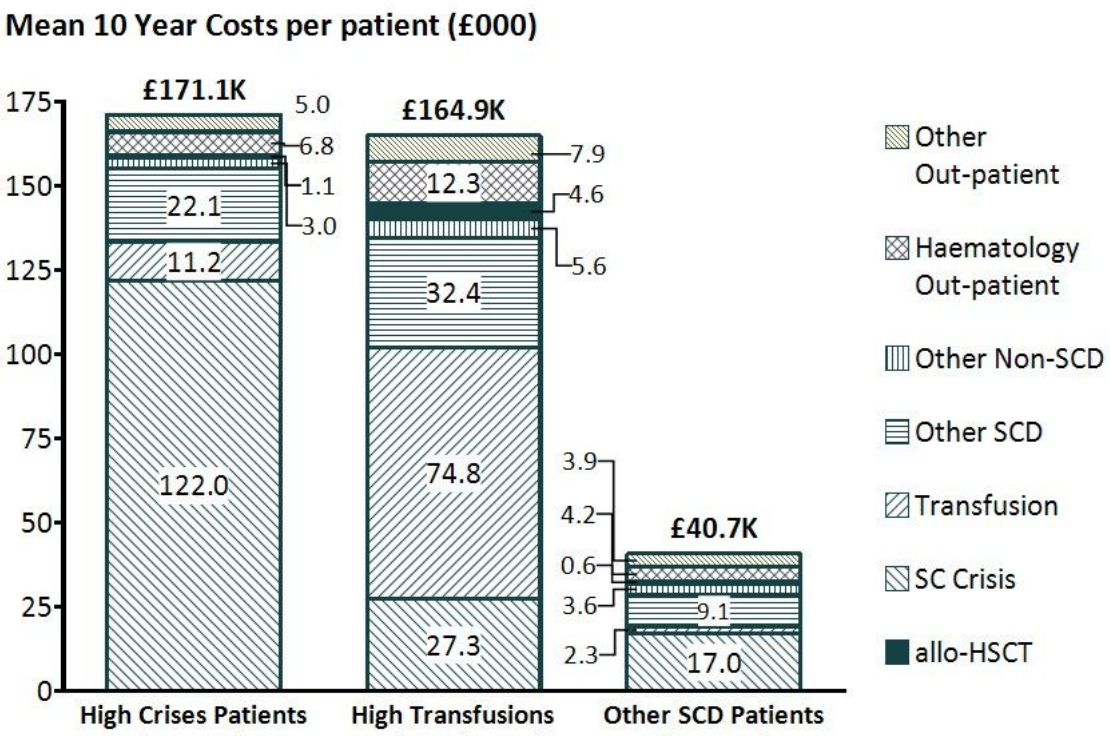
Hospital costs by treatment type for all SCD patients by year, 2009-2018.



	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	
High Crises Patients Costs	1,194	1,194	1,312	1,428	1,462	1,469	1,557	1,578	1,613	1,713	4.1%
High Transfusions Patients Costs	205	205	257	319	367	419	458	553	570	589	12.1%
Other SCD Patients Costs	8,464	8,628	8,650	8,636	8,670	8,698	8,621	8,520	8,452	8,268	-0.3%
Total Patients	**9,863**	**10,027**	**10,219**	**10,383**	**10,499**	**10,586**	**10,636**	**10,651**	**10,635**	**10,570**	0.8%

Figure 2

Annual hospital costs and patient numbers by sub-groups by year, 2009-2018.



Mean Annual Cost:	High Crises Patients (n=1,194)	High Transfusions Patients (n=205)	Other SCD Patients (n=8,464)
2009-2010	**£16.8K**	**£14.2K**	**£2.4K**
2011-2018	**£17.2K**	**£17.1K**	**£4.4K**

Figure 3

10-year hospital costs by 2009/2010 patient sub-group.